# WEST Search History

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| | | *DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR* | |
| ☐ | L52 | (lipoprotein)same(T)adj(cell)adj(signaling) | 0 |
| ☐ | L51 | (Apo-1)same(T)adj(cell)adj(signaling) | 0 |
| ☐ | L50 | L49 and (apo)adj(A-1)adj(fragment) | 0 |
| ☐ | L49 | L40 and (monocyte) | 87 |
| ☐ | L48 | L46 and AFTI | 0 |
| ☐ | L47 | L46 and (apo)adj(A-1) | 0 |
| ☐ | L46 | L45 and monocyte? | 26 |
| ☐ | L45 | L44 and IL-1 | 27 |
| ☐ | L44 | L43 and TNF | 30 |
| ☐ | L43 | L42 and (T)adj(cell)adj(activation) | 39 |
| ☐ | L42 | L41 and inhibit | 127 |
| ☐ | L41 | L40 and fragment | 145 |
| ☐ | L40 | L36 and (apolipoprotein) | 147 |
| ☐ | L39 | L36 and (apolipoprotein)adj(A-I)adj(fragment) | 0 |
| ☐ | L38 | L36 and Apo-A | 0 |
| ☐ | L37 | L36 and Apo-A-I | 0 |
| ☐ | L36 | 424/185.1,192.1,193.1,280.1,134.1,436/529,530/359,514/57,59.ccls. | 4648 |
| ☐ | L35 | 424/185.1,192.1,193.1,134.1 | 0 |
| ☐ | L34 | 424/185.1,192.1,193.1,280.1,134.1 | 0 |
| ☐ | L33 | 424/185.1,192.1,193.1,280.1,134.1,436/529,530/359,514/57,59 | 0 |
| ☐ | L32 | L30 and apo-A-I | 5 |
| ☐ | L31 | L30 and apo-A | 0 |
| ☐ | L30 | 424/185.1 192.1, 134.1.ccls. | 6358 |
| ☐ | L29 | L28 and apo-A | 0 |
| ☐ | L28 | L27 and lipoprotein | 31 |
| ☐ | L27 | L26 and (IL-1) | 107 |
| ☐ | L26 | L25 and (TNF)adj(alpha) | 144 |
| ☐ | L25 | L24 and (monocyte) | 312 |
| ☐ | L24 | L23 and (signaling) | 509 |
| ☐ | L23 | L21 and (T)adj(cell) | 2309 |
| ☐ | L22 | L21 and apo-A-I | 0 |

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| ☐ | L21 | (424/185.1 \|424/192.1 \|424/134.1).ccls. | 3460 |
| ☐ | L20 | L14 and (T)adj(cell)adj(signaling) | 11 |
| ☐ | L19 | L14 and apo-A-I | 21 |
| ☐ | L18 | L14 and (TNF)same(IL1) | 12 |
| ☐ | L17 | L14 and anti-inflammation | 1 |
| ☐ | L16 | L15 and anti-inflammation | 1 |
| ☐ | L15 | L14 and inflammation | 333 |
| ☐ | L14 | (human)adj(apolipoprotein) | 1018 |
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| ☐ | L12 | (apo-A-I)same(fragment) | 10 |
| ☐ | L11 | (edwards)adj(carl)adj(k) | 20 |
| ☐ | L10 | (kohno)adj(tadahiko) | 23 |
| ☐ | L9 | (burger)adj(danielle) | 1 |
| ☐ | L8 | (dayer)adj(jean)adj(michel) | 5 |
| | *DB=USPT; PLUR=YES; OP=OR* | | |
| ☐ | L7 | 5786206.pn. | 1 |
| ☐ | L6 | 6518412.pn. | 1 |
| ☐ | L5 | 6844327.pn. | 1 |
| ☐ | L4 | 6897039.pn. | 1 |
| ☐ | L3 | 5876968.pn. | 1 |
| ☐ | L2 | 5786206.pn. | 1 |
| | *DB=PGPB; PLUR=YES; OP=OR* | | |
| ☐ | L1 | 20020064820 | 1 |

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| NEWS 4 | DEC 18 | CA/CAplus patent kind codes updated |
| NEWS 5 | DEC 18 | MARPAT to CA/CAplus accession number crossover limit increased to 50,000 |
| NEWS 6 | DEC 18 | MEDLINE updated in preparation for 2007 reload |
| NEWS 7 | DEC 27 | CA/CAplus enhanced with more pre-1907 records |
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| NEWS 18 | FEB 23 | KOREAPAT enhanced with IPC 8 features and functionality |
| NEWS 19 | FEB 26 | MEDLINE reloaded with enhancements |
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| NEWS 22 | FEB 26 | IFICDB/IFIPAT/IFIUDB reloaded with enhancements |
| NEWS 23 | FEB 26 | CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases |
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| NEWS 25 | MAR 16 | CASREACT coverage extended |
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| NEWS EXPRESS | NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006. |
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=> s apolipoprotein fragment
L1          39 APOLIPOPROTEIN FRAGMENT

=> s l1 and T cell
L2           0 L1 AND T CELL

=> s l1 and monocyte
L3           0 L1 AND MONOCYTE

=> s l1 and TNF
L4           0 L1 AND TNF

=> s l1 and apo-A-I
L5           0 L1 AND APO-A-I

=> dup remove l1
PROCESSING COMPLETED FOR L1
L6           20 DUP REMOVE L1 (19 DUPLICATES REMOVED)

=> d l6 1-20 cbib abs

L6   ANSWER 1 OF 20     MEDLINE on STN                  DUPLICATE 1
2004148472.     PubMed ID: 14663630.   Preparation and investigation of 99m
     technetium-labeled low-density lipoproteins in rabbits with experimentally
     induced hypercholesterolemia. Bozoky Z; Balogh L; Mathe D; Fulop L; Bertok
     L; Janoki Gy A. (Fodor Jozsef National Center of Public Health, FJC
     National Research Institute for Radiobiology and Radiohygiene, P.O.B. 101,
     1775 Budapest, Hungary.. bozoky@hp.osski.hu) . European biophysics journal
     : EBJ, (2004 Apr) Vol. 33, No. 2, pp. 140-5.  Electronic Publication:
     2003-12-09. Journal code: 8409413. ISSN: 0175-7571. Pub. country: Germany:
     Germany, Federal Republic of. Language: English.
AB   Low-density lipoproteins (LDL) were radiolabeled in atherosclerosis
     studies.  The aim was to investigate the biodistribution and uptake of
     99mTc-labeled LDL by atherosclerotic plaques in experimentally induced
     hyperlipidemia.  Rabbits were fed a diet containing 2% cholesterol for 60
     days to develop hyperlipidemia and atheromatous aortic plaques.  A
     combination of preparative and analytical ultracentrifugation was used to
     investigate human LDL aliquots, to prepare radioactive-labeled
     lipoproteins and in rabbits with induced hyperlipidemia.  Preparative
     density gradient centrifugation was applied for the simultaneous isolation
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of the major lipoprotein density classes, which form discrete bands of lipoproteins in the preparative tubes. The cholesterol and protein levels in the lipoprotein fractions were determined. LDL was subsequently dialysed against physiological solution and sterilized and apolipoprotein fragments and aggregates were eliminated by passage through a 0.22-micron filter. LDL was radiolabeled with 99mTc by using sodium dithionite as a reducing agent. Radiochemical purity and in vitro stability were controlled by paper chromatography in acetone. The labelling efficiency was 85-90% for human LDL. Two months after the start of cholesterol feeding, the total cholesterol in the blood serum had increased approximately 33-fold in comparison with the basal cholesterol content of hypercholesterolemic rabbits. Investigation of LDL was performed by Schlieren analysis after adjustment of the density of serum and underlayering by salt solution in a spinning ultracentrifugation capillary band-forming cell. Quantitative results were obtained by measuring the Schlieren areas between the sample curves and the reference baseline curve by means of computerized numerical and graphic techniques. In this manner we measured the concentrations of human LDL and analyzed rabbit LDL levels in induced hyperlipidemia. Gamma scintillation camera scanning of the rabbits was performed. Overnight fasted rabbits were injected in the marginal ear vein with 99mTc-labeled human LDL (4-10 mCi, 0.5-1.5 mg protein). The initial scintigram showing a typical blood-pool scan, gradually changing with time to an image of specific organ uptake of radioactivity by the liver, kidneys and brain and in the bladder. Gamma camera in vivo scintigraphy on rabbits revealed visible signals corresponding to atherosclerotic plaques in the aorta and carotid arteries. Our results show that 99mTc-LDL can be used to assess the organ distribution pattern of LDL in the rabbit, and to detect and localize areas of arterial atherosclerotic lesions.

L6 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
2003:376646 Document No. 138:348741 Neuronal steroid content-affecting agents for treating lesions of the nervous system. Pfrieger, Frank W.; Mauch, Daniela; Goritz, Christian; Nagler, Karl (Max-Delbrueck-Centrum Fuer Molekulare Medizin, Germany). PCT Int. Appl. WO 2003039555 A2 20030515, 9 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2002-DE4140 20021107. PRIORITY: DE 2001-10154221 20011107.
AB The invention discloses agents and methods which influence the steroid content of neurons in order to increase the survival rate of neurons and to regenerate synapses after lesions of the nervous system. The invention also discloses the use of components of the nervous system that play a role in the steroid metabolism for diagnosing lesions.

L6 ANSWER 3 OF 20 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2003:420108 Document No.: PREV200300420108. Relationship of non-LDL-bound apo(a), urinary apo(a) fragments and plasma Lp(a) in patients with impaired renal function. Cauza, Edmund; Kletzmaier, Josef; Bodlaj, Gert; Dunky, Attila; Herrmann, Wolfgang; Kostner, Karam [Reprint Author]. Department of Cardiology, AKH Wien, Waehringerguertel 18-20, A-1090, Vienna, Austria. karamkostner@hotmail.com. Nephrology Dialysis Transplantation, (August 2003) Vol. 18, No. 8, pp. 1568-1572. print. ISSN: 0931-0509 (ISSN print). Language: English.
AB Background. Plasma lipoprotein (a) (Lp(a)) has been shown to be a risk factor for atherosclerosis in numerous studies. However, the catabolism of this lipoprotein is not very clear. We and others have shown that Lp(a) is excreted into urine in the form of fragments. Lp(a) has also been shown to exist in a low-density non-lipoprotein (LDL)-bound form. Since Lp(a) is increased in all forms of kidney disease with reduced

excretory kidney function and decreased excretion of apo(a) fragments could be partially responsible for this increase, we investigated the relationship of non-LDL-bound apo(a), urinary apo(a) fragments and plasma Lp(a) in patients with impaired renal function. Methods. Plasma Lp(a), non-LDL-bound apo(a) and urinary apo(a) fragments were measured in 55 kidney disease patients (28 males and 27 females) and matched controls. Results. Plasma Lp(a) and non-LDL-bound apo(a) were increased in patients, whereas urinary apo(a) was decreased, especially in patients with a creatinine clearance < 70 ml/min. There was a significant correlation between plasma Lp(a) and non-LDL-bound apo(a) in patients and controls. Conclusion. We conclude that decreased urinary apo(a) excretion could be one possible mechanism of increased plasma Lp(a) and non-LDL-bound apo(a) in patients with decreased kidney function.

L6 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

2003:474451 Document No. 139:243394 Increased microvascular permeability in the hamster cheek pouch induced by oxidized low density lipoprotein (oxLDL) and some fragmented apolipoprotein B proteins. Svensjoe, E.; Boschcov, P.; Ketelhuth, D. F. J.; Jancar, S.; Gidlund, M. (Laboratorio de Imunologia Molecular, Instituto Biofisica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil). Inflammation Research, 52(5), 215-220 (English) 2003. CODEN: INREFB. ISSN: 1023-3830. Publisher: Birkhaeuser Verlag.

AB Oxidized low-d. lipoproteins (oxLDL) and protein fractions obtained by size exclusion chromatog. of oxLDL were tested for vascular permeability effects on topical application to the hamster cheek pouch. The hamster cheek pouch was prepared for intravital microscopy observations of macromol. leakage at post capillary venules (= leaks) with FITC-dextran as tracer. OxLDL (0.1 mg/mL), PAF (platelet activation factor, 50-100 nM) and protein fractions of oxLDL (10 μg/mL) were applied topically to hamster cheek pouches. Application of oxLDL and PAF resulted in reversible increases in the number of leaks. The PAF-antagonist WEB 2170, L-NAME and a β2-adrenoceptor agonist inhibited ($P<0.01$) almost completely the macromol. leakage induced with oxLDL or PAF. Protein fractions were found to be more effective than unfractionated oxLDL in inducing plasma leakage as calculated on mg/mL-basis. Hamster oxLDL is a potent inducer of macro-mol. leakage increase in the hamster cheek pouch microcirculation. The principal effect is mediated by PAF-like structures produced by the oxidation of the LDL-particle but oxLDL also contains low mol. weight proteins that could contribute to the overall vascular permeability increasing effect of ox LDL.

L6 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

2003:70348 Document No. 138:385721 Synthesis, conformation and vibrational dynamics of the peptide -Ser-Cys-Lys-Leu-Asp-Phe-, a fragment of apolipoprotein B. Srivastava, Shinoo; Srivastava, Seema; Melkani, Girish Chandra; Singh, Shyam; Gupta, Vishwambhar Dayal; Gupta, Vijai Prakash (Division of Physiology, Central Drug Research Institute, Lucknow, 226 001, India). Indian Journal of Biochemistry & Biophysics, 39(6), 410-418 (English) 2002. CODEN: IJBBBQ. ISSN: 0301-1208. Publisher: National Institute of Science Communication and Information Resources.

AB The collective normal modes of the hexapeptide -Ser-Cys-Lys-Leu-Asp-Phe-, a fragment of apolipoprotein B (apo B), have been obtained. They reflect the dynamic nature and are at least partly responsible for energy input in autolytic activity. Further, on energetic considerations based on the measurements reported by Sim & Sim (1984), it has been shown that of the two such fragments only one induces autolysis, while the other remains anchored to the coated pit.

L6 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

2000:68487 Document No. 132:132339 Polypeptide derivatives as angiogenesis inhibitors. Smith, Richard Anthony Godwin; Bright, Jeremy Richard; Steward, Michael; Cox, Vivienne Frances (Adprotech PLC, UK). PCT Int. Appl. WO 2000004052 A2 20000127, 36 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES,

FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB2292 19990716. PRIORITY: GB 1998-15505 19980716.

AB It has been found that derivs. of angiogenesis inhibiting proteins may be prepared in which a neg. feedback process can be enhanced for therapeutic purposes and which can be targeted to cell membranes and sites of active angiogenesis particularly those of the vascular endothelium. The invention provides a soluble derivative of a polypeptide capable of inhibiting angiogenesis, said derivative comprising a combination of heterologous membrane binding elements covalently associated with the polypeptide so that the derivative acquires affinity for the surface of the vascular endothelium particularly that of growing blood vessels. The soluble polypeptide may be selected from the non-catalytic regions of human plasminogen (within the N-terminal 560 residues of that protein); fragments thereof, particularly those generated by metalloprotease digestion of plasminogen; fragments of related proteins containing kringle domains such as hepatocyte growth factor or apolipoprotein (a), prothrombin, tissue-type plasminogen activator, urinary-type plasminogen activator and hybrids thereof with plasminogen sequences; mutants of the above kringle domains, those containing pos. charged to neutral or neg. charged mutations at positions 20, 21, 78 and 79; fragments of collagen, particularly collagen XVIII; fragments of prolactin, the 16kDa N-terminal region of prolactin; neutralizing antibodies against receptors for angiogenic mediators; antagonists of integrins involved in angiogenesis; and hybrids, derivs. or muteins thereof. Each membrane binding element with low membrane affinity may have a dissociation constant of 1 μM-1 mM, and the derivative may incorporate sufficient elements with low affinities for membrane components to result in a 0.01-10 nM dissociation constant affinity for specific membranes.

L6 ANSWER 7 OF 20 MEDLINE on STN DUPLICATE 2

1998062920. PubMed ID: 9398171. Infrared spectroscopy of human apolipoprotein fragments in SDS/D2O: relative lipid-binding affinities and a novel amide I assignment. Shaw R A; Buchko G W; Wang G; Rozek A; Treleaven W D; Mantsch H H; Cushley R J. (Institute for Biodiagnostics, National Research Council of Canada, Winnipeg, Manitoba, Canada.. shaw@ibd.nrc.ca) . Biochemistry, (1997 Nov 25) Vol. 36, No. 47, pp. 14531-8. Journal code: 0370623. ISSN: 0006-2960. Pub. country: United States. Language: English.

AB Infrared absorption spectra are reported for six apolipoprotein fragments in SDS/D2O. Five of the peptides correspond to proposed lipid-binding domains of human apolipoproteins [apoC-I(7-24), apoC-I(35-53), apoA-II(18-30)+, apoA-I(166-185), apoE(267-289)], and the sixth is the de novo lipid associating peptide LAP-20. The amide I infrared absorption patterns are generally consistent with predominantly helical structures (as determined previously by NMR spectroscopy and distance geometry calculations) and further suggest that apoA-I(166-185) and apoE(267-289) are bound to SDS relatively weakly in comparison to the other four peptides. The latter conclusion is also supported by the temperature dependence of the infrared spectra, as increasing temperature promotes a distinct increase in random coil structure only for apoA-I(166-185) and apoE(267-289). In addition to features readily ascribed to helices, the infrared spectra of all the peptides show absorptions in the spectral region 1630-1635 cm-1 that is usually associated with beta-structure, a motif that is clearly absent from the NMR-derived structures. Parallel difficulties also arose in the analyses of the circular dichroism spectra. We suggest that both the low-frequency infrared absorptions and the ambiguities in interpreting the CD spectra may be due to unusual structures at the peptide C-termini, involving C=O groups that form hydrogen bonds simultaneously either with two solvent molecules or with donors from the backbone (NH) and the solvent (OH). Analogous absorptions may be a general feature of solvent-exposed helices,

which suggests a need for caution in assigning amide I bands below 1640 cm-1.

L6 ANSWER 8 OF 20 MEDLINE on STN DUPLICATE 3
96339306. PubMed ID: 8756691. Conformations of human apolipoprotein E(263-286) and E(267-289) in aqueous solutions of sodium dodecyl sulfate by CD and 1H NMR. Wang G; Pierens G K; Treleaven W D; Sparrow J T; Cushley R J. (Institute of Molecular Biology and Biochemistry, Simon Fraser University, Burnaby, British Columbia, Canada. ) Biochemistry, (1996 Aug 13) Vol. 35, No. 32, pp. 10358-66. Journal code: 0370623. ISSN: 0006-2960. Pub. country: United States. Language: English.
AB Structures of apoE(263-286) and apoE(267-289) have been determined in aqueous solution containing 90-fold molar excess of perdeuterated sodium dodecyl sulfate by CD and 1H NMR. Conformations were calculated by distance geometry based on 370 and 276 NOE distance restraints, respectively. RMSD for superimposing the region 265-284 from an ensemble of 41 structures for apoE(263-286) is 0.64 +/- 0.17 A for backbone atoms (N, C alpha, C = O) and 1.51 +/- 0.13 A for all atoms. The backbone RMSD for an ensemble of 37 structures for apoE(267-289) is 0.74 +/- 0.21 A for the region 268-275 and 0.34 +/- 0.10 A for the region 276-286. A two-domain structure was found for apoE(267-289) with the C-terminal half adopting a very well defined helix and the N-terminal segment 268-275 a less well defined helix, suggesting that the N-terminus may weakly bind to SDS. For apoE(263-286), an amphipathic helix-bend-helix structural motif was found with all hydrophobic side chains on the concave face. The existence of a bend around residues Q273 to G278 is consistent with their temperature coefficients of amide protons as well as secondary shifts of alpha-protons. Comparison of the structures of the two peptides revealed that the enhanced binding of apoE(263-286) to lipid could be attributed to the formation of a hydrophobic cluster consisting of residues W264, F265, L268, and V269. Aromatic side chains are proposed to be especially important in anchoring apolipoprotein fragments to micelles.

L6 ANSWER 9 OF 20 MEDLINE on STN DUPLICATE 4
96129536. PubMed ID: 8576649. Components of the protein fraction of oxidized low density lipoprotein stimulate interleukin-1 alpha production by rabbit arterial macrophage-derived foam cells. Lipton B A; Parthasarathy S; Ord V A; Clinton S K; Libby P; Rosenfeld M E. (Department of Medicine, University of California San Diego, La Jolla, USA. ) Journal of lipid research, (1995 Oct) Vol. 36, No. 10, pp. 2232-42. Journal code: 0376606. ISSN: 0022-2275. Pub. country: United States. Language: English.
AB Oxidized low density lipoproteins (oxLDL) (0.5-50 micrograms/ml) generated from both rabbit and human LDL stimulated the production of interleukin-1 alpha (IL-1 alpha) by as much as 2- and 6-fold, respectively, as compared to native LDL after a 2-h incubation with macrophage-derived foam cells isolated from the balloon-injured arteries of cholesterol-fed rabbits. Northern blot analyses confirmed that there was also an increase in the mRNA for IL-1 alpha and IL-beta in response to oxLDL in the isolated foam cells. The stimulation of IL-1 expression and production was not due to the contamination of the oxLDL preparations with endotoxin as neither the amount of endotoxin found to be associated with the lipoproteins nor amounts up to 1 ng/ml stimulated IL-1 alpha production to the same degree as oxLDL. Neither oxidized beta-very low density lipoprotein (VLDL) nor oxidized high density lipoprotein (HDL) stimulated IL-1 alpha production by the foam cells. Furthermore, acetyl-LDL had a very limited stimulatory effect, but other known ligands of the scavenger receptor such as maleylated-BSA, polyinosinic acid, and fucoidin elicited maximal IL-1 alpha responses. Fractionation of the oxLDL into lipid- and protein-soluble fractions showed that there was some stimulatory activity in the lipid phase but that known products of lipid peroxidation such as 9- and 13-HODE had no effect when added independently of lipoproteins. When added in combination with native LDL, only 13-HODE stimulated IL-1 alpha production. The delipidated apolipoprotein fragments of oxLDL that had been solubilized in

beta-octylglucoside stimulated the production of IL-1 alpha by the foam cells to a greater degree than the lipid extract, while reductively methylated oxLDL did not. These data suggest that interactions of components of both the lipid- and protein-soluble fractions of oxLDL with scavenger receptors or potentially with surface proteins that bind oxLDL may induce production of IL-1 by arterial macrophages.

L6 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
1991:604835 Document No. 115:204835 Molecular parameters that control the association of low density lipoprotein apo B-100 with chondroitin sulfate. Olsson, Urban; Camejo, German; Olofsson, Sven Olof; Bondjers, Goeran (Dep. Med., Univ. Goeteborg, Goeteborg, S-413 45, Swed.). Biochimica et Biophysica Acta, Molecular Basis of Disease, 1097(1), 37-44 (English) 1991. CODEN: BBADEX. ISSN: 0925-4439.
AB The association of low d. lipoprotein (LDL) with proteoglycans of the arterial intima, in particular chondroitin 6-sulfate proteoglycans, may contribute to LDL accumulation during atherogenesis. The authors studied the interactions of apolipoprotein B-100 (apo B-100) peptide segments and model peptides with chondroitin 6-sulfate. The ability of these peptides to inhibit complex formation between LDL and chondroitin 6-sulfate was used as a measurement of the interaction. Results from earlier studies suggest that surface-localized segments of apo B-100 are responsible for the interaction of LDL with heparin and chondroitin sulfate-rich arterial proteoglycans. Therefore 16 hydrophilic apo B-100 peptides were selected for studies and synthesized with a peptide synthesizer. These synthetic peptides were 7 to 26 amino acids long. Four of the peptides inhibited the association of LDL with chondroitin 6-sulfate, namely apo B segments 4230-4254, 3359-3377, 3145-3157 and 2106-2121. The 3359-3377 segment was the most efficient. A common feature between the interacting peptides was an excess of pos. charged side chains and based on these results the authors synthesized 9 model peptides that shared sequence characteristics with the interacting apo B-100 peptides. Five of these: RSGRKRSGK, RSSRKRSGK, RGGRKRGGK, RSRSRSRSR and RGRGRGRGR were shown to block the LDL-chondroitin-6-sulfate association, with RSRSRSRSR being the most effective. The results suggest that the optimal association of the peptides with chondroitin 6-sulfate is obtained with a minimal chain length of 9 amino acids and a min. of 5 pos. charges and that flexibility in the binding region is important.

L6 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
1990:511477 Document No. 113:111477 C-Terminal domain of apolipoprotein CII as both activator and competitive inhibitor of lipoprotein lipase. Cheng, Qi; Blackett, Piers; Jackson, Kenneth W.; McConathy, Walter J.; Wang, Chi Sun (Health Sci. Cent., Univ. Oklahoma, Oklahoma City, OK, 73104, USA). Biochemical Journal, 269(2), 403-7 (English) 1990. CODEN: BIJOAK. ISSN: 0306-3275.
AB Peptides of the C-terminal domain of apolipoprotein C-II (apoC-II) were prepared by a solid-peptide-synthesis technique and it was demonstrated that the C-terminal tetrapeptide, Lys-Gly-Glu-Glu, represents an inhibitor of lipoprotein lipase (I). The tetrapeptide not only inhibited the basal activity of I, but also blocked the activation effect of native apoC-II. The lengthening of this tetrapeptide resulted in a corresponding increase in affinity for I. This suggested that amino acids other than those of the C-terminal tetrapeptide also contribute to the binding affinity of apoC-II for I. On the basis of an essential requirement of the apoC-II terminal domain for binding to I, the initial interaction of apoC-II, mediated via the C-terminal tetrapeptide, was suggested to promote the proper alignment of apoC-II with I, followed by the weak interaction of the apoC-II activator domain with the I activator site, enhancing the lipolysis process.

L6 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
1986:437677 Document No. 105:37677 Studies to determine the receptor binding domain of apolipoprotein-B100. Chapman, M. John; Innerarity, Thomas L.; Jacobson, Shellie; Mahley, Robert W. (Hop. Pitie, Paris, 75671, Fr.).

International Congress Series, 681(Diabetes, Obes. Hyperlipidemias-3), 103-11 (English) 1985. CODEN: EXMDA4. ISSN: 0531-5131.

AB The binding site on the apolipoprotein-B100 for the apolipoprotein B,E (low-d. lipoprotein) receptor was investigated. To determination the receptor-binding activity of various groups of the apolipoprotein, tryptic fragments were prepared and reconstituted into low-d. lipid particles by recombination with lipids. The recombinant particles obtained were spherical, heterogeneous, and .apprx.200-800 Å in dilution The apolipoprotein low-d.-lipid recombinant bound to the apolipoprotein B,E receptor of cultured human fibroblasts. Since the recombinants contained most of the apolipoprotein fragments, it was not possible to make any correlation as to which group was responsible for binding. Studies with monoclonal antibodies to apolipoprotein B inhibited binding to receptor; antibody 18C4 gave 60-80% inhibition. The apolipoprotein B fragments reacting with 18C4 were identified as 22,000- and 24,000-mol.-weight tryptic fragment.

L6 ANSWER 13 OF 20 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 5

82076865 EMBASE Document No.: 1982076865. Serum and urinary lipoproteins in the human nephrotic syndrome: evidence for renal catabolism of lipoproteins. Shore V.G.; Forte T.; Licht H.; Lewis S.B.. Biomed. Sci. Div., Lawrence Livermore Nat. Lab., L-452, Livermore, CA 94550, United States. Metabolism: Clinical and Experimental Vol. 31, No. 3, pp. 258-268 1982.
CODEN: METAAJ
Pub. Country: United States. Language: English.
Entered STN: 911209. Last Updated on STN: 911209

AB The urinary excretion of lipoproteins and the possibility of catabolic alterations on glomerular filtration were investigated in four nephrotic subjects differing in etiology, serum lipoprotein profile, and 24 hr urinary output of protein and lipids. The apolipoproteins and lipoproteins of urine were compared with those of serum with respect to distribution profile, physical properties, and composition. Lipoprotein particles resembling the serum very low, intermediate, low and high density lipoproteins (VLDL, IDL, LDL, and HDL, respectively) in density, particle size, and morphology were isolated from the urine. As expected from molecular sieving effects during glomerular filtration, the urinary HDL were more abundant than the lower density lipoproteins even when the plasma LDL was elevated markedly. However, little sieving effect was seen within the urinary HDL, which comprised a broad spectrum of particle sizes including the larger HDL2, whose average diameter was similar to that of the plasma HDL. A sieving effect was not seen in the urinary LDL, except for a greatly increased proportion, about 20% of total particles, of HDL-like species. Intact apolipoproteins were not found in the concentrated urinary fraction isolated by ultrafiltration between the limits of 104 and 5 x 104 daltons. On the basis of immunoreactivity, gel electrophoresis and amino acid composition, apolipoproteins B and AI are the major and minor proteins, respectively, of urinary LDL, and apo B is the major protein of the urinary IDL and VLDL. Apolipoproteins AI, AII, CI, CIII, and possibly AIV were isolated from the urinary HDL. As much as 20% of the protein moiety of the urinary HDL appeared to be large apolipoprotein fragments with molecular weights and isoelectric points similar to those of apo CII and apo CIII. The fragments were derived in part from apo AI, the least acidic form of which was lost preferentially. The lower density classes of urinary lipoproteins also appeared to have lost apo E and apo C's and to have undergone partial proteolysis. Apparently, the surface-exposed, readily exchangeable apolipoproteins are subject to proteolytic degradation upon glomerular filtration.

L6 ANSWER 14 OF 20 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

1980:208659 The Genuine Article (R) Number: JP627. PHOSPHOLIPID BINDING-STUDIES WITH SYNTHETIC APOLIPOPROTEIN FRAGMENTS***.

SPARROW J T (Reprint); GOTTO A M. BAYLOR UNIV, COLL MED, HOUSTON, TX 77030; METHODIST HOSP, HOUSTON, TX 77030. FEDERATION PROCEEDINGS (1980) Vol. 39, No. 6, pp. 1977-1977. ISSN: 0014-9446. Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA. Language: English.

L6 ANSWER 15 OF 20 MEDLINE on STN DUPLICATE 6
80240471. PubMed ID: 6772077. Phospholipid binding studies with synthetic apolipoprotein fragments. Sparrow J T; Gotto A M Jr.
Annals of the New York Academy of Sciences, (1980) Vol. 348, pp. 187-211. Ref: 41. Journal code: 7506858. ISSN: 0077-8923. Pub. country: United States. Language: English.

L6 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
1979:147614 Document No. 90:147614 Lecithin:cholesterol acyltransferase activation and lipid binding by synthetic fragments of apolipoprotein C-I. Soutar, A. K.; Sigler, G. F.; Smith, L. C.; Gotto, A. M., Jr.; Sparrow, James T. (Dep. Med., Baylor Coll. Med., Houston, TX, USA). Scandinavian Journal of Clinical and Laboratory Investigation, Supplement, 38(150), 53-8 (English) 1978. CODEN: SCLSAH. ISSN: 0085-591X.
AB Peptide fragments of apolipoprotein C-I (apoC-I) were synthesized by solid-phase methods. After purification, each peptide showed the correct amino acid anal. and was a single band on polyacrylamide gel electrophoresis. In d. gradient ultracentrifugation with vesicles of dimyristoylphosphatidylcholine, peptide fragments 32-57, 24-57, and 17-57 formed stable complexes, whereas fragment 39-57 did not. With mixed vesicles of dimyristoylphosphatidylcholine-cholesterol, 20 μM of fragments 32-57, 24-57, and 17-57 stimulated lecithin-cholesterol acyltransferase (I) activity 50, 60, and 100% resp., of the value found for apoC-I, whereas fragment 39-57 was inactive. The results indicate that residues 17-57 contain the structural requirements for I activation by apoC-I, and that residues 32-57 represent one of the major phospholipid-binding regions of apoC-I.

L6 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
1976:593106 Document No. 85:193106 An improved polystyrene support for solid phase peptide synthesis. Sparrow, James T. (Dep. Med., Baylor Coll. Med., Houston, TX, USA). Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp., 4th, 419-24. Editor(s): Walter, Roderich; Meienhofer, Johannes. Ann Arbor Sci.: Ann Arbor, Mich. (English) 1975. CODEN: 33UYAW.
AB P-(R1-OCH2)C6H4CH2CONH(CH2)10CONH(CH2)10CONHCH2C6H4-R2-p (R1 = amino acid residues, R2 = polystyrene resin) was prepared from chloromethylated polystyrene. Using this resin Phe-Ser-Glu-Phe-Trp-Asp-Leu-Asp-Pro-Glu-Val-Arg-Pro-Thr-Ser-Ala-Val-Ala-Ala, the sequence 61-79 of apolipoprotein C-III of human serum, was prepared in 28.9% overall yield.

L6 ANSWER 18 OF 20 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 7
1975:166986 The Genuine Article (R) Number: AB111. INTERCONVERSIONS OF APOLIPOPROTEIN FRAGMENTS. BLUM C B (Reprint); LEVY R I.
NHLI, MOLEC DIS BRANCH, BETHESDA, MD 20014. ANNUAL REVIEW OF MEDICINE (1975) Vol. 26, pp. 365-371. ISSN: 0066-4219. Publisher: ANNUAL REVIEWS INC, 4139 EL CAMINO WAY, PO BOX 10139, PALO ALTO, CA 94303-0139. Language: English.

L6 ANSWER 19 OF 20 MEDLINE on STN
75203748. PubMed ID: 167648. Interconversions of apolipoproteins fragments. Blum C B; Levy R I. Annual review of medicine, (1975) Vol. 26, pp. 345-71. Ref: 53. Journal code: 2985151R. ISSN: 0066-4219. Pub. country: United States. Language: English.

L6 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
1973:25634 Document No. 78:25634 Cystine-containing apolipoprotein of human plasma high density lipoproteins. Characterization of cyanogen bromide and tryptic fragments. Jackson, Richard L.; Gotto, Antonio M. (Dep. Med.,

Methodist Hosp., Houston, TX, USA). Biochimica et Biophysica Acta, Protein Structure, 285(1), 36-47 (English) 1972. CODEN: BBPTBH. ISSN: 0005-2795.

AB A major protein (or apolipoprotein) constituent has been isolated from human plasma high density lipoproteins and shown to contain 2 monomeric units covalently linked by a single SS bond. The protein is designated apoLP-Gln-II, based on its C-terminal amino acid. It contains no histidine, arginine, or tryptophan and is also devoid of carbohydrate. Amino acid anal. of reduced-aminoethylated apoLP-Gln-II indicates 77 residues and a single methionine per monomeric unit. Two unique CNBr fragments, CNBr III and IV, have been isolated from the reduced-aminoethylated protein and account for all of the 77 amino acids of the monomer. CNBr IV has 26 residues, a blocked N-terminus, no isoleucine, 1 residue of aminoethylcysteine, C-terminal homoserine and corresponds therefore to the N-terminal and cystine-containing portion of apoLP-Gln-II. CNBr III has 51 amino acids, including 1 residue of isoleucine, has C-terminal glutamine, has no aminoethylcysteine and corresponds to the C-terminus of apoLP-glutamine-II. CNBr III and IV have each been digested with trypsin and the resulting peptides isolated by a combination of gel filtration and ion-exchange chromatog. Twelve tryptic fragments accounted for the 77 amino acids present in apoLP-Gln-II. This finding and the tryptic fingerprint anal. of reduced-aminoethylated apoLP-Gln-II indicate that apoLP-Gln-II must contain 2 identical or very nearly identical subunits.

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=> s apolipoprotein A-I
L7       27002 APOLIPOPROTEIN A-I

=> s l7 and fragment
L8        1253 L7 AND FRAGMENT

=> s l8 and monocytes
L9          14 L8 AND MONOCYTES

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10            8 DUP REMOVE L9 (6 DUPLICATES REMOVED)

=> d l10 1-8 cbib abs
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L10 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

2006:13229 Document No. 144:101036 Antibody and antisense polynucleotide modulating genes differentially expressed in polycystic disorders for treating polycystic diseases. McPherson, John M.; Beskrovnaya, Oxana (Genzyme Corporation, USA). PCT Int. Appl. WO 2006002203 A2 20060105, 78 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-US21994 20050623. PRIORITY: US 2004-582673P 20040623; US 2004-582875P 20040625.

AB This invention provides compns. and methods to diagnose and treat polycystic disorders by inhibiting the biol. activity of a gene now correlated with appearance of this disorder. By way of illustrative only, the tissue growth factor-alpha (TGF-α) gene is an example of such a gene. Also provided are antibody, antisense polynucleotide, ribozyme, and multivalent RNA aptamer to treat or ameliorate abnormal cystic lesions and diseases associated with the formation of cysts in tissue. The methods and compns. treat and ameliorate pathol. cyst formation in tissue by inhibiting or augmenting gene expression or the biol. activity the gene.

expression product, or its receptor.

L10 ANSWER 2 OF 8 MEDLINE on STN
2005696094. PubMed ID: 16251720. Cell surface-expressed moesin-like HDL/apoA-I binding protein promotes cholesterol efflux from human macrophages. Matsuyama Akifumi; Sakai Naohiko; Hiraoka Hisatoyo; Hirano Ken-ichi; Yamashita Shizuya. (Medical Center for Translational Research, Osaka University Hospital, 2-15 Yamada-oka, Suita. ) Journal of lipid research, (2006 Jan) Vol. 47, No. 1, pp. 78-86. Electronic Publication: 2005-10-26. Journal code: 0376606. ISSN: 0022-2275. Pub. country: United States. Language: English.

AB HDL and its major component, apolipoprotein A-I (apoA-I), play a central role in reverse cholesterol transport. We recently reported the involvement of a glycosylphosphatidylinositol anchor (GPI anchor) in the binding of HDL and apoA-I on human macrophages, and purified an 80 kDa HDL/apoA-I binding protein. In the present study, we characterized the GPI-anchored HDL/apoA-I binding protein from macrophages. The HDL/apoA-I binding protein was purified from macrophages and digested with endopeptidase, and the resultant fragments were sequenced. Cholesterol efflux, flow cytometry, immunoblotting, and immunohistochemical analyses were performed to characterize the HDL/apoA-I binding protein. Two parts of seven amino acid sequences completely matched those of moesin. Flow cytometry, immunoblotting, and immunohistochemistry using anti-moesin antibody showed that the HDL/apoA-I binding protein was N-glycosylated and expressed on the cell surface. It was termed moesin-like protein. Treatment of macrophages with anti-moesin antibody blocked the binding of HDL/apoA-I and suppressed cholesterol efflux. The moesin-like protein was exclusively expressed on macrophages and was upregulated by cholesterol loading and cell differentiation. Our results indicate that the moesin-like HDL/apoA-I binding protein is specifically expressed on the surface of human macrophages and promotes cholesterol efflux from macrophages.-Matsuyama, A, N. Sakai, H. Hiraoka, K-i. Hirano, and S. Yamashita. Cell surface-expressed moesin-like HDL/apoA-I binding protein promotes cholesterol efflux from human macrophages.

L10 ANSWER 3 OF 8 MEDLINE on STN DUPLICATE 1
2004517173. PubMed ID: 15487703. Degradation of pre-beta-high density lipoproteins and their binding activity to human blood monocytes . Nakabayashi Tetsuo; Yamauchi Kazuyoshi; Sugano Mitsutoshi; Sano Kenji; Tozuka Minoru; Hidaka Hiroya. (Department of Laboratory Medicine, School of Medicine, Shinshu University, Matsumoto, Nagano, Japan. ) Annals of clinical and laboratory science, (2004 Summer) Vol. 34, No. 3, pp. 287-98. Journal code: 0410247. ISSN: 0091-7370. Pub. country: United States. Language: English.

AB We have previously reported that high density lipoprotein3 (HDL3), apolipoprotein A-I (apoA-I) rich lipoprotein, binds specifically to the surface of human blood monocytes. Pre-beta-HDL with a pre-beta mobility on agarose gels is an apoA-I (MW 28 kDa)-rich and a lipid-poor lipoprotein. In the present study, we found that pre-beta-HDL purified by ion-exchange chromatography was susceptible to degradation if isolated in the absence of anti-proteases, resulting in the smaller lyso-pre-beta-HDL. The mass of lyso-pre-beta-HDL was confirmed using a delayed extraction matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (DE-MALDI-TOF MS), which showed a fragment of approximately 22,378.9 Da. We further investigated limited proteolysis of apo A-I purified from human plasma HDL with various proteases, and cleavage appeared to be limited to the C-terminal end of apo A-I (amino acids 188-223). The ability of pre-beta-HDL and lyso-pre-beta-HDL to compete for HDL binding to monocytes was determined using a flow cytometry-based assay. Pre-beta-HDL competed efficiently for binding whereas lyso-pre-beta-HDL was significantly less effective. The data may indicate that the binding sites on monocytes specifically recognize apoA-I. We suggest that limited proteolysis around amino acids 188-223 of apo A-I may affect

lipid binding, which may in turn affect HDL structure and function.

L10 ANSWER 4 OF 8 MEDLINE on STN DUPLICATE 2
2002284668. PubMed ID: 12027302. The saga of the discovery of IL-1 and TNF and their specific inhibitors in the pathogenesis and treatment of rheumatoid arthritis. Dayer Jean-Michel. (Division of Immunology and Allergy, University Hospital, Geneva, Switzerland.. jean-michel.dayer@hcuge.ch) . Joint, bone, spine : revue du rhumatisme, (2002 Mar) Vol. 69, No. 2, pp. 123-32. Ref: 76. Journal code: 100938016. ISSN: 1297-319X. Pub. country: France. Language: English.

AB In the seventies, the molecule subsequently termed IL-1 was among the first cytokines to attract the attention of rheumatologists due to its biological role in tissue destruction and bone resorption. In the mid-eighties, cachectin/tumor necrosis factor was found to share some of these biological activities, and a strong synergism between the two cytokines became evident. While IL-1 appeared to be more important at the local level, TNF played a more prominent part at the systemic level. In 1984, we became aware of the existence of an antagonist to IL-1 - subsequently termed IL-1Ra (interleukin-1 receptor antagonist) - in urine of febrile patients; its mechanism of action was elucidated in 1987 and the molecule cloned in 1990. The natural inhibitors of TNF were identified in 1996/97 by different investigators and proved to be soluble fragments of the TNF receptor. A concept commonly accepted at present is that disease activity and clinical outcome are controlled by the balance between agonistic and antagonistic cytokines, and at present the principal goal is to understand the underlying mechanisms. This concept is illustrated by observations in numerous animal models. The control of IL-1 and TNF is strongly dependent on the contact between activated lymphocytes and monocytes, the main source of these cytokines. Inhibiting this interaction by interfering with ligands and counter-ligands may be a useful approach if it is possible to maintain the production of the cytokine antagonist. Apolipoproteins A-I and A-II as well as beta2-integrins are molecules that block ligand/counter-ligand interaction. According to animal experiments and clinical data, blocking either IL-1 or TNF, or both, is beneficial. However, to determine not only the benefit but also the side effects of combination therapy in the human system, long-term clinical trials will be required.

L10 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
2001:693510 Document No. 135:271905 Apolipoprotein A-I and its fragments regulate T-cell-dependent monocyte activation. Edwards, Carl K., III; Burger, Danielle; Dayer, Jean-Michel; Kohno, Tadahiko (Amgen Inc., USA). PCT Int. Appl. WO 2001068852 A2 20010920, 132 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US7826 20010313. PRIORITY: US 2000-PV189008 20000313.

AB The invention provides apolipoprotein A-I fragment T cell activation inhibitor (AFTI) polypeptides and nucleic acid mols. encoding the same. Apolipoprotein and its fragments are shown to regulate T-cell mediated activation of monocytes via the inhibition of interleukin-1β and tumor necrosis factor-α secretion. A fragment of apo-A-I comprising domains II and III also displays inhibitory activity. The invention also provides vectors, host cells, selective binding agents, and methods for producing AFTI polypeptides. Also provided are methods for the treatment, diagnosis, amelioration, or prevention of diseases with AFTI polypeptides, particularly IL-1 mediated diseases, TNF-α

mediated diseases, and diseases involving monocyte activation.

L10 ANSWER 6 OF 8 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

1999:109868 The Genuine Article (R) Number: 163NY. Lipoproteins inhibit macrophage activation by lipoteichoic acid. Grunfeld C (Reprint); Marshall M; Shigenaga J K; Moser A H; Tobias P; Feingold K R. Univ Calif San Francisco, Dept Med, San Francisco, CA 94121 USA (Reprint); Dept Vet Affairs Med Ctr, Med Serv, Metab Sect, San Francisco, CA 94121 USA; Scripps Res Inst, Dept Immunol, La Jolla, CA 92037 USA. JOURNAL OF LIPID RESEARCH (FEB 1999) Vol. 40, No. 2, pp. 245-252. ISSN: 0022-2275. Publisher: LIPID RESEARCH INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA. Language: English.

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Regulation of lipid metabolism during infection is thought to be part of host defense, as lipoproteins neutralize endotoxin (LPS) and viruses. Gram-positive infections also induce disturbances in lipid metabolism. Therefore, we investigated whether lipoproteins could inhibit the toxic effects of lipoteichoic acid (LTA), a fragment of gram-positive bacteria. LTA activated RAW264.7 macrophage cells, stimulating production of tumor necrosis factor (TNF) in a dose-dependent matter, but produced less TNF than that seen after LPS activation. High density (HDL) or low density lipoprotein (LDL) alone inhibited the ability of LPS to stimulate TNF production, but had little effect on the activation by LTA, When a maximally effective dose of LTA was mixed with lipoproteins and 10% lipoprotein-depleted plasma (LPDP), the ability of LTA to stimulate macrophage production of TNF was inhibited. HDL, LDL, and the synthetic particle, Soyacal, when mixed with LPDP, were able to inhibit the ability of LTA to activate macrophages, Lipopolysaccharide-binding protein (LBP) substituted for LPDP in catalyzing lipoprotein neutralization of LTA by HDL, Antibody to LBP inhibited the ability of LPDP to induce LTA neutralization by HDL. Thus, lipoproteins can prevent macrophage activation by fragments from both gram-positive and gram-negative microorganisms.

L10 ANSWER 7 OF 8 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

1998:78187 Document No.: PREV199800078187. Serum amyloid A (SAA) protein enhances formation of cyclooxygenase metabolites of activated human monocytes. Malle, Ernst [Reprint author]; Bollmann, Andreas; Steinmetz, Armin; Gemsa, Diethard; Leis, Hans-Jorg; Sattler, Wolfgang. Karl-Franzens Univ. Graz, Inst. Med. Biochem., Harrachgasse 21, A-8010 Graz, Austria. FEBS Letters, (Dec. 15, 1997) Vol. 419, No. 2-3, pp. 215-219. print.

CODEN: FEBLAL. ISSN: 0014-5793. Language: English.

AB As serum amyloid A (SAA), an apolipoprotein associated with HDL during the acute-phase reaction may induce Ca2+ mobilization in human monocytes we raised the question whether SAA1 the predominant isoform of human acute-phase SAA is able to alter eicosanoid formation. In resting monocytes SAA1 was without effect on the secretion of cyclooxygenase metabolites while in calcium ionophore A23187-(0.5 and 2.5 muM) stimulated cells SAA1 led to a pronounced dose-dependent increase of TXA2, PGE2, and PGF2alpha. In addition a time-dependent increase of cyclooxygenase metabolites in between 1.5- and 3-fold in the presence of SAA1 was observed; apo A-I, the main HDL-apolipoprotein under nonacute-phase conditions, had no effect. Using sequence-specific anti-human SAA1 peptide (40-63) F(ab)2 fragments we could show that the proposed Ca2+-binding tetrapeptide Gly48-Pro49-Gly50-Gly51 of SAA1 is not responsible for enhanced biosynthesis of cyclooxygenase metabolites. Finally, we could demonstrate that human SAA1 is unable to bind Ca2+-ions, suggesting that SAA1 does not directly enhance eicosanoid biosynthesis via Ca2+ mobilization leading to enhanced phospholipase A2 activity.

L10 ANSWER 8 OF 8 MEDLINE on STN

95169050. PubMed ID: 7864806. Phospholipase A2 from plasma of patients

with septic shock is associated with high-density lipoproteins and C3 anaphylatoxin: some implications for its functional role. Gijon M A; Perez C; Mendez E; Sanchez Crespo M. (Departamento de Bioquimica y Fisiologia-Consejo Superior de Investigaciones Cientificas, Facultad de Medicina, Valladolid, Spain. ) The Biochemical journal, (1995 Feb 15) Vol. 306 ( Pt 1), pp. 167-75. Journal code: 2984726R. ISSN: 0264-6021. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Phospholipase A2 (PLA2) activity was purified 12,544-fold with a 13% yield from the plasma of patients diagnosed of septic shock by the sequential use of heparin-agarose affinity chromatography, gel filtration, and reverse-phase f.p.l.c. Gel-filtration chromatography of plasma omitting high-ionic-strength buffer revealed a molecular mass different from that of purified PLA2 and co-elution with apolipoprotein A-I peaks, which suggests its association with high-density lipoproteins (HDL). N-terminal analysis of the enzyme activity protein band, electroblotted from a SDS-acrylamide gel and with an assessed molecular mass of 19 kDa, showed an identical sequence to that of alpha-chain of human C3 complement component, suggesting the presence in this band of a complex formed by a complement C3-derived anaphylatoxin (C3a)-related fragment and the PLA2 linked side-by-side. Because the preparation of plasma enzyme showed lower activity than the enzyme obtained from fibroblasts transfected with the coding sequence of human group-II PLA2, and because the addition of C3-derived anaphylatoxins from human serum inhibited the activity of this recombinant PLA2, it was considered that C3a-related peptides behave as inhibitors of group-II PLA2. The enzyme showed optimal activity on [14C]oleate-labelled autoclaved E. coli, on synthetic phosphatidylethanolamine, and on [3H]arachidonate-labelled membranes of the monoblast cell line U937, but it did not show any activity on the release of [3H]arachidonate from pre-labelled human polymorphonuclear leukocytes (PMNs). In short, PLA2 from plasma of sepsis patients shows unique associations with other plasma proteins which may influence its functional properties. The association with C3-related peptides shows an inhibitory effect on the enzyme activity, whereas the association with HDL might influence its environment and/or its interaction with cells. The study of the catalytic properties shows a prominent effect on bacterial phospholipids, synthetic phosphatidylethanolamine, and membranes from U937 monoblasts, but not on synthetic phosphatidylcholine or on PMNs, even when these cells were maintained in culture to allow spontaneous apoptosis and became a good substrate for pancreatic type PLA2.

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     (FILE 'HOME' ENTERED AT 17:18:34 ON 21 MAR 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 17:18:51 ON
     21 MAR 2007
L1            39 S APOLIPOPROTEIN FRAGMENT
L2             0 S L1 AND T CELL
L3             0 S L1 AND MONOCYTE
L4             0 S L1 AND TNF
L5             0 S L1 AND APO-A-I
L6            20 DUP REMOVE L1 (19 DUPLICATES REMOVED)
L7         27002 S APOLIPOPROTEIN A-I
L8          1253 S L7 AND FRAGMENT
L9            14 S L8 AND MONOCYTES
L10            8 DUP REMOVE L9 (6 DUPLICATES REMOVED)

=> s l8 and TNF
L11            8 L8 AND TNF

=> dup remove l11
PROCESSING COMPLETED FOR L11
L12            6 DUP REMOVE L11 (2 DUPLICATES REMOVED)
```

=> d l12 1-6 cbib abs

L12 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
2002:716529 Document No. 137:261388 Probe microarrays for detection of genes and alleles associated with risk of arteriosclerosis. Cullen, Paul; Seedorf, Udo (Ogham G.m.b.h., Germany). PCT Int. Appl. WO 2002072882 A2 20020919, 146 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2002-EP2780 20020313. PRIORITY: DE 2001-10111925 20010313.

AB A microarray hybridization method for determining the genetic component of the risk of arteriosclerosis in a patient is described. The array uses probes derived from reference sequences and from alleles of genes known to be associated with increased risk of arteriosclerosis. Anal. of the hybridization pattern is used to assess the risk for the patient.

L12 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
2002:676043 Document No. 137:213257 Increased recovery of active proteins using a reduction/oxidation coupling reagent. Sassenfeld, Helmut M.; Remmele, Richard L., Jr.; McCoy, Rebecca E. (Immunex Corporation, USA). PCT Int. Appl. WO 2002068455 A2 20020906, 38 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US5645 20020222. PRIORITY: US 2001-271033P 20010223.

AB The invention provides methods of increasing yields of desired conformation of proteins. In particular embodiments, the invention includes contacting prepns. of a recombinant protein with a reduction/oxidation coupling reagent for a time sufficient to increase the relative proportion of a desired configurational isomer. A TNF receptor-Fc fusion protein fraction with low TNF binding activity was treated with a redox coupling system of reduced glutathione and glutathione to drive the inactive form to the active conformation.

L12 ANSWER 3 OF 6 MEDLINE on STN DUPLICATE 1
2002284668. PubMed ID: 12027302. The saga of the discovery of IL-1 and TNF and their specific inhibitors in the pathogenesis and treatment of rheumatoid arthritis. Dayer Jean-Michel. (Division of Immunology and Allergy, University Hospital, Geneva, Switzerland.. jean-michel.dayer@hcuge.ch) . Joint, bone, spine : revue du rhumatisme, (2002 Mar) Vol. 69, No. 2, pp. 123-32. Ref: 76. Journal code: 100938016. ISSN: 1297-319X. Pub. country: France. Language: English.

AB In the seventies, the molecule subsequently termed IL-1 was among the first cytokines to attract the attention of rheumatologists due to its biological role in tissue destruction and bone resorption. In the mid-eighties, cachectin/tumor necrosis factor was found to share some of these biological activities, and a strong synergism between the two cytokines became evident. While IL-1 appeared to be more important at the local level, TNF played a more prominent part at the systemic level. In 1984, we became aware of the existence of an antagonist to IL-1 - subsequently termed IL-1Ra (interleukin-1 receptor antagonist) - in urine of febrile patients; its mechanism of action was elucidated in 1987 and the molecule cloned in 1990. The natural inhibitors of TNF

were identified in 1996/97 by different investigators and proved to be soluble fragments of the TNF receptor. A concept commonly accepted at present is that disease activity and clinical outcome are controlled by the balance between agonistic and antagonistic cytokines, and at present the principal goal is to understand the underlying mechanisms. This concept is illustrated by observations in numerous animal models. The control of IL-1 and TNF is strongly dependent on the contact between activated lymphocytes and monocytes, the main source of these cytokines. Inhibiting this interaction by interfering with ligands and counter-ligands may be a useful approach if it is possible to maintain the production of the cytokine antagonist. Apolipoproteins A-I and A-II as well as beta2-integrins are molecules that block ligand/counter-ligand interaction. According to animal experiments and clinical data, blocking either IL-1 or TNF, or both, is beneficial. However, to determine not only the benefit but also the side effects of combination therapy in the human system, long-term clinical trials will be required.

L12 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
2001:693510 Document No. 135:271905 Apolipoprotein A-I and its fragments regulate T-cell-dependent monocyte activation. Edwards, Carl K., III; Burger, Danielle; Dayer, Jean-Michel; Kohno, Tadahiko (Amgen Inc., USA). PCT Int. Appl. WO 2001068852 A2 20010920, 132 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US7826 20010313. PRIORITY: US 2000-PV189008 20000313.

AB The invention provides apolipoprotein A-I fragment T cell activation inhibitor (AFTI) polypeptides and nucleic acid mols. encoding the same. Apolipoprotein and its fragments are shown to regulate T-cell mediated activation of monocytes via the inhibition of interleukin-1β and tumor necrosis factor-α secretion. A fragment of apo-A-I comprising domains II and III also displays inhibitory activity. The invention also provides vectors, host cells, selective binding agents, and methods for producing AFTI polypeptides. Also provided are methods for the treatment, diagnosis, amelioration, or prevention of diseases with AFTI polypeptides, particularly IL-1 mediated diseases, TNF-α mediated diseases, and diseases involving monocyte activation.

L12 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
2000:368631 Document No. 133:13378 Tumor necrosis factor receptor 2 (TNF-R2) gene as a marker for a complex polygenic disease. Morris, Brian J. (The University of Sydney, Australia). PCT Int. Appl. WO 2000031293 A1 20000602, 50 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-AU1050 19991125. PRIORITY: AU 1998-7323 19981125.

AB The present invention relates to a method of identifying a gene or a linked gene region responsible for contributing for causation of a complex polygenic disease in a patient, and for predicting the general susceptibility to a complex polygenic disease including coronary artery disease, essential hypertension, hyperlipidemia, non-insulin dependent diabetes mellitus, or diabetic neuropathy. The method comprises determination of

the genotype of the individual for a polymorphism in the TNFRSF1B gene that encodes tumor necrosis factor receptor 2 (TNF-R2), wherein the presence of one allele of the polymorphism is indicative of an increased risk over an individual with a contrasting allele of the polymorphism.

L12 ANSWER 6 OF 6 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

1999:109868 The Genuine Article (R) Number: 163NY. Lipoproteins inhibit macrophage activation by lipoteichoic acid. Grunfeld C (Reprint); Marshall M; Shigenaga J K; Moser A H; Tobias P; Feingold K R. Univ Calif San Francisco, Dept Med, San Francisco, CA 94121 USA (Reprint); Dept Vet Affairs Med Ctr, Med Serv, Metab Sect, San Francisco, CA 94121 USA; Scripps Res Inst, Dept Immunol, La Jolla, CA 92037 USA. JOURNAL OF LIPID RESEARCH (FEB 1999) Vol. 40, No. 2, pp. 245-252. ISSN: 0022-2275. Publisher: LIPID RESEARCH INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA. Language: English.

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Regulation of lipid metabolism during infection is thought to be part of host defense, as lipoproteins neutralize endotoxin (LPS) and viruses. Gram-positive infections also induce disturbances in lipid metabolism. Therefore, we investigated whether lipoproteins could inhibit the toxic effects of lipoteichoic acid (LTA), a fragment of gram-positive bacteria. LTA activated RAW264.7 macrophage cells, stimulating production of tumor necrosis factor (TNF) in a dose-dependent matter, but produced less TNF than that seen after LPS activation. High density (HDL) or low density lipoprotein (LDL) alone inhibited the ability of LPS to stimulate TNF production, but had little effect on the activation by LTA, When a maximally effective dose of LTA was mixed with lipoproteins and 10% lipoprotein-depleted plasma (LPDP), the ability of LTA to stimulate macrophage production of TNF was inhibited. HDL, LDL, and the synthetic particle, Soyacal, when mixed with LPDP, were able to inhibit the ability of LTA to activate macrophages, Lipopolysaccharide-binding protein (LBP) substituted for LPDP in catalyzing lipoprotein neutralization of LTA by HDL, Antibody to LBP inhibited the ability of LPDP to induce LTA neutralization by HDL. Thus, lipoproteins can prevent macrophage activation by fragments from both gram-positive and gram-negative microorganisms.

=> s l8 and IL-1
L13 5 L8 AND IL-1

=> dup remove l13
PROCESSING COMPLETED FOR L13
L14 3 DUP REMOVE L13 (2 DUPLICATES REMOVED)

=> d l14 1-3 cbib abs

L14 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

2004:183769 Document No. 140:372427 Relationship between the gene polymorphism of interleukin-1α (-889) and the plasma lipoprotein level in healthy population. Huang, He; Li, Yan; Xu, Pu; Zhang, Pingan; Li, Gengshan (Renmin Hospital, Wuhan University, Wuhan, 430060, Peop. Rep. China). Wuhan Daxue Xuebao, Yixueban, 24(2), 99-101 (Chinese) 2003. CODEN: WDXYAA. ISSN: 1671-8852. Publisher: Wuhan Daxue Xuebao, Yixueban Faxingbu.

AB The gene polymorphism at the position-889 in the promoter of interleukin (IL)-1 alpha was analyzed by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP), and the plasma lipoprotein level was inspected in 184 healthy Chinese Han Population of Hubei simultaneously. The plasma lipoprotein level, including total cholesterol (TC), triglycerides (TG), high-d. lipoprotein cholesterol (HDL-C), low-d. lipoprotein cholesterol (LDL-C), apolipoprotein A1 (apoA1), and apolipoprotein B (apoB), was not

significantly different among different genotypes of IL-1.alpha. (-889). There is no relationship between the gene polymorphism of IL-1.alpha. (-889) and the plasma lipoprotein level in healthy Chinese Han Population of Hubei.

L14 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 1

2002284668. PubMed ID: 12027302. The saga of the discovery of IL-1 and TNF and their specific inhibitors in the pathogenesis and treatment of rheumatoid arthritis. Dayer Jean-Michel. (Division of Immunology and Allergy, University Hospital, Geneva, Switzerland.. jean-michel.dayer@hcuge.ch) . Joint, bone, spine : revue du rhumatisme, (2002 Mar) Vol. 69, No. 2, pp. 123-32. Ref: 76. Journal code: 100938016. ISSN: 1297-319X. Pub. country: France. Language: English.

AB In the seventies, the molecule subsequently termed IL-1 was among the first cytokines to attract the attention of rheumatologists due to its biological role in tissue destruction and bone resorption. In the mid-eighties, cachectin/tumor necrosis factor was found to share some of these biological activities, and a strong synergism between the two cytokines became evident. While IL-1 appeared to be more important at the local level, TNF played a more prominent part at the systemic level. In 1984, we became aware of the existence of an antagonist to IL-1 - subsequently termed IL-1Ra (interleukin-1 receptor antagonist) - in urine of febrile patients; its mechanism of action was elucidated in 1987 and the molecule cloned in 1990. The natural inhibitors of TNF were identified in 1996/97 by different investigators and proved to be soluble fragments of the TNF receptor. A concept commonly accepted at present is that disease activity and clinical outcome are controlled by the balance between agonistic and antagonistic cytokines, and at present the principal goal is to understand the underlying mechanisms. This concept is illustrated by observations in numerous animal models. The control of IL-1 and TNF is strongly dependent on the contact between activated lymphocytes and monocytes, the main source of these cytokines. Inhibiting this interaction by interfering with ligands and counter-ligands may be a useful approach if it is possible to maintain the production of the cytokine antagonist. Apolipoproteins A-I and A-II as well as beta2-integrins are molecules that block ligand/counter-ligand interaction. According to animal experiments and clinical data, blocking either IL-1 or TNF, or both, is beneficial. However, to determine not only the benefit but also the side effects of combination therapy in the human system, long-term clinical trials will be required.

L14 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

2001:693510 Document No. 135:271905 Apolipoprotein A-I and its fragments regulate T-cell-dependent monocyte activation. Edwards, Carl K., III; Burger, Danielle; Dayer, Jean-Michel; Kohno, Tadahiko (Amgen Inc., USA). PCT Int. Appl. WO 2001068852 A2 20010920, 132 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US7826 20010313. PRIORITY: US 2000-PV189008 20000313.

AB The invention provides apolipoprotein A-I fragment T cell activation inhibitor (AFTI) polypeptides and nucleic acid mols. encoding the same. Apolipoprotein and its fragments are shown to regulate T-cell mediated activation of monocytes via the inhibition of interleukin-1β and tumor necrosis factor-α secretion. A fragment of apo-A-I comprising domains II and III also displays inhibitory activity. The invention also

provides vectors, host cells, selective binding agents, and methods for producing AFTI polypeptides. Also provided are methods for the treatment, diagnosis, amelioration, or prevention of diseases with AFTI polypeptides, particularly IL-1 mediated diseases, TNF-α mediated diseases, and diseases involving monocyte activation.

=> s (dayer j?/au or burger d?/au or kohno t?/au or edwards III c?/au)
L15 8081 (DAYER J?/AU OR BURGER D?/AU OR KOHNO T?/AU OR EDWARDS III C?/AU )

=> s l15 and apolipoprotein A-I
L16 43 L15 AND APOLIPOPROTEIN A-I

=> s l16 and fragment
L17 5 L16 AND FRAGMENT

=> dup remove l17
PROCESSING COMPLETED FOR L17
L18 3 DUP REMOVE L17 (2 DUPLICATES REMOVED)

=> d l18 1-3 cbib abs

L18 ANSWER 1 OF 3 MEDLINE on STN DUPLICATE 1
2002284668. PubMed ID: 12027302. The saga of the discovery of IL-1 and TNF and their specific inhibitors in the pathogenesis and treatment of rheumatoid arthritis. Dayer Jean-Michel. (Division of Immunology and Allergy, University Hospital, Geneva, Switzerland.. jean-michel.dayer@hcuge.ch) . Joint, bone, spine : revue du rhumatisme, (2002 Mar) Vol. 69, No. 2, pp. 123-32. Ref: 76. Journal code: 100938016. ISSN: 1297-319X. Pub. country: France. Language: English.

AB In the seventies, the molecule subsequently termed IL-1 was among the first cytokines to attract the attention of rheumatologists due to its biological role in tissue destruction and bone resorption. In the mid-eighties, cachectin/tumor necrosis factor was found to share some of these biological activities, and a strong synergism between the two cytokines became evident. While IL-1 appeared to be more important at the local level, TNF played a more prominent part at the systemic level. In 1984, we became aware of the existence of an antagonist to IL-1 - subsequently termed IL-1Ra (interleukin-1 receptor antagonist) - in urine of febrile patients; its mechanism of action was elucidated in 1987 and the molecule cloned in 1990. The natural inhibitors of TNF were identified in 1996/97 by different investigators and proved to be soluble fragments of the TNF receptor. A concept commonly accepted at present is that disease activity and clinical outcome are controlled by the balance between agonistic and antagonistic cytokines, and at present the principal goal is to understand the underlying mechanisms. This concept is illustrated by observations in numerous animal models. The control of IL-1 and TNF is strongly dependent on the contact between activated lymphocytes and monocytes, the main source of these cytokines. Inhibiting this interaction by interfering with ligands and counter-ligands may be a useful approach if it is possible to maintain the production of the cytokine antagonist. Apolipoproteins A-I and A-II as well as beta2-integrins are molecules that block ligand/counter-ligand interaction. According to animal experiments and clinical data, blocking either IL-1 or TNF, or both, is beneficial. However, to determine not only the benefit but also the side effects of combination therapy in the human system, long-term clinical trials will be required.

L18 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
2001:798252 Document No. 135:362518 Apo-AI/AII peptide derivatives for hypocholesteremic and antiviral therapy. Kohno, Tadahiko (Amgen Inc., USA). PCT Int. Appl. WO 2001081376 A2 20011101, 49 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US13068 20010423. PRIORITY: US 2000-PV198920 20000421.

AB The present invention concerns therapeutic agents that mimic the activity of Apo-AI amphipathic helix peptide. In accordance with the present invention, the compds. of the invention comprise: (a) a Apo-AI amphipathic helix peptide or Apo-AI amphipathic helix peptide-mimetic domain, preferably the amino acid sequence of SEQ ID NO:7, or sequences derived therefrom by phage display, RNA-peptide screening, or the other techniques mentioned above; and (b) a vehicle, such as a polymer (e.g., PEG or dextran) or an Fc domain, which is preferred; wherein the vehicle, preferably an Fc domain, is covalently attached to the Apo-AI amphipathic helix peptide or Apo-AI amphipathic helix peptide-mimetic domain. The vehicle and the Apo-AI amphipathic helix peptide or Apo-AI amphipathic helix peptide-mimetic domain may be linked through the N- or C-terminus of the Apo-AI amphipathic helix peptide or Apo-AI amphipathic helix peptide-mimetic domain, as described further below. The preferred vehicle is an Fc domain, and the preferred Fc domain is an IgG Fc domain. Preferred Apo-AI amphipathic helix peptide or Apo-AI amphipathic helix peptide-mimetic domains comprise the amino acid sequences described in Table 1. Other Apo-AI amphipathic helix peptide or Apo-AI amphipathic helix peptide-mimetic domains can be generated by phage display, RNA-peptide screening and the other techniques mentioned herein.

L18 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

2001:693510 Document No. 135:271905 Apolipoprotein A-I and its fragments regulate T-cell-dependent monocyte activation. Edwards, Carl K., III; Burger, Danielle; Dayer, Jean-Michel; Kohno, Tadahiko (Amgen Inc., USA). PCT Int. Appl. WO 2001068852 A2 20010920, 132 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US7826 20010313. PRIORITY: US 2000-PV189008 20000313.

AB The invention provides apolipoprotein A-I fragment T cell activation inhibitor (AFTI) polypeptides and nucleic acid mols. encoding the same. Apolipoprotein and its fragments are shown to regulate T-cell mediated activation of monocytes via the inhibition of interleukin-1β and tumor necrosis factor-α secretion. A fragment of apo-A-I comprising domains II and III also displays inhibitory activity. The invention also provides vectors, host cells, selective binding agents, and methods for producing AFTI polypeptides. Also provided are methods for the treatment, diagnosis, amelioration, or prevention of diseases with AFTI polypeptides, particularly IL-1 mediated diseases, TNF-α mediated diseases, and diseases involving monocyte activation.

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 NEWS  5  DEC 18  MARPAT to CA/CAplus accession number crossover limit increased
                  to 50,000
 NEWS  6  DEC 18  MEDLINE updated in preparation for 2007 reload
 NEWS  7  DEC 27  CA/CAplus enhanced with more pre-1907 records
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 NEWS 20  FEB 26  EMBASE enhanced with Clinical Trial Number field
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 NEWS 25  MAR 16  CASREACT coverage extended
 NEWS 26  MAR 20  MARPAT now updated daily
 NEWS 27  MAR 22  LWPI reloaded

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COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

=> s human apolipoprotein A-I
L1         1678 HUMAN APOLIPOPROTEIN A-I

=> s l1 and truncation
L2           25 L1 AND TRUNCATION

=> dup remove l2
PROCESSING COMPLETED FOR L2
L3             9 DUP REMOVE L2 (16 DUPLICATES REMOVED)

=> d l3 1-9 cbib abs

L3   ANSWER 1 OF 9  SCISEARCH  COPYRIGHT (c) 2007 The Thomson Corporation  on
     STN
2007:195177   The Genuine Article (R) Number: 133CP. Conformation and lipid
     binding of a C-terminal (198-243) peptide of human
     apolipoprotein A-I.  Zhu H L; Atkinson D
     (Reprint). Boston Univ, Sch Med, Dept Physiol & Biophys, W308, 715 Albany
     St, Boston, MA 02118 USA (Reprint); Boston Univ, Sch Med, Dept Physiol &
     Biophys, Boston, MA 02118 USA. Atkinson@bu.edu. BIOCHEMISTRY (13 FEB 2007)
     Vol. 46, No. 6, pp. 1624-1634. ISSN: 0006-2960. Publisher: AMER CHEMICAL
     SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA. Language: English.
     *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
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AB Human apolipoprotein A-I (apoA-I) is the principle apolipoprotein of high-density lipoproteins that are critically involved in reverse cholesterol transport. The intrinsically flexibility of apoA-I has hindered studies of the structural and functional details of the protein. Our strategy is to study peptide models representing different regions of apoA-I. Our previous report on [1-44]apoA-I demonstrated that this N-terminal region is unstructured and folds into similar to 60% alpha-helix with a moderate lipid binding affinity. We now present details of the conformation and lipid interaction of a C-terminal 46-residue peptide, [198-243]apoA-I, encompassing putative helix repeats 10 and 9 and the second half of repeat 8 from the C-terminus of apoA-I. Far-ultraviolet circular dichroism spectra show that [198-243]apoA-I is also unfolded in aqueous solution. However, self-association induces similar to 50% alpha-helix in the peptide. The self-associated peptide exists mainly as a tetramer, as determined by native electrophoresis, cross-linking with glutaraldehyde, and unfolding data from circular dichroism (CD) and differential scanning calorimetry (DSC). In the presence of a number of lipid-mimicking detergents, above their CMC, similar to 60% alpha-helix was induced in the peptide. In contrast, SDS, an anionic lipid-mimicking detergent, induced helical folding in the peptide at a concentration of similar to 0.003% (similar to 100 mu M), similar to 70-fold below its typical CMC (0.17-0.23% or 6-8 mM). Both monomeric and tetrameric peptide can solubilize dimyristoylphosphatidylcholine (DMPC) liposomes and fold into similar to 60% alpha-helix. Fractionation by density gradient ultracentrifugation and visualization by negative staining electromicroscopy demonstrated that the peptide binds to DMPC with a high affinity to form at least two sizes of relatively homogeneous discoidal HDL-like particles depending on the initial lipid:peptide ratio. The characteristics (lipid:peptide weight ratio, diameter, and density) of both complexes are similar to those of plasma A-I/DMPC complexes formed under similar conditions: small discoidal complexes (similar to 3:1 weight ratio, similar to 110 A, and similar to 1.10 g/cm(3)) formed at an initial 1:1 weight ratio and larger discoidal complexes (similar to 4.6:1 weight ratio, similar to 165 A, and similar to 1.085 g/cm(3)) formed at initial 4:1 weight ratio. The cross-linking data for the peptide on the complexes of two sizes is consistent with the calculated peptide numbers per particle. Compared to the similar to 100 A disk-like complex formed by the N-terminal peptide in which helical structure was insufficient to cover the disk edge by a single belt, the compositions of these two types of complexes formed by the C-terminal peptide are more consistent with a "double belt" model, similar to that proposed for full-length apoA-I. Thus, our data provide direct evidence that this C-terminal region of apoA-I is responsible for the self-association of apoA-I, and this C-terminal peptide model can mimic the interaction with the phospholipid of plasma apoA-I to form two sizes of homogeneous discoidal complexes and thus may be responsible for apoA-I function in the formation and maintenance of HDL subspecies in plasma.

L3 ANSWER 2 OF 9 MEDLINE on STN DUPLICATE 1

2006092979. PubMed ID: 16452169. Crystal structure of human apolipoprotein A-I: insights into its protective effect against cardiovascular diseases. Ajees A Abdul; Anantharamaiah G M; Mishra Vinod K; Hussain M Mahmood; Murthy H M Krishna. (Center for Biophysical Sciences and Engineering and Atherosclerosis Research Unit and Department of Medicine, University of Alabama, 1530 3rd Avenue South, Birmingham, AL 35294, USA. ) Proceedings of the National Academy of Sciences of the United States of America, (2006 Feb 14) Vol. 103, No. 7, pp. 2126-31. Electronic Publication: 2006-02-01. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB Despite three decades of extensive studies on human apolipoprotein A-I (apoA-I), the major protein component in high-density lipoproteins, the molecular basis for its antiatherogenic function is elusive, in part because of lack of a

structure of the full-length protein. We describe here the crystal structure of lipid-free apoA-I at 2.4 A. The structure shows that apoA-I is comprised of an N-terminal four-helix bundle and two C-terminal helices. The N-terminal domain plays a prominent role in maintaining its lipid-free conformation, indicating that mutants with truncations in this region form inadequate models for explaining functional properties of apoA-I. A model for transformation of the lipid-free conformation to the high-density lipoprotein-bound form follows from an analysis of solvent-accessible hydrophobic patches on the surface of the structure and their proximity to the hydrophobic core of the four-helix bundle. The crystal structure of human apoA-I displays a hitherto-unobserved array of positively and negatively charged areas on the surface. Positioning of the charged surface patches relative to hydrophobic regions near the C terminus of the protein offers insights into its interaction with cell-surface components of the reverse cholesterol transport pathway and antiatherogenic properties of this protein. This structure provides a much-needed structural template for exploration of molecular mechanisms by which human apoA-I ameliorates atherosclerosis and inflammatory diseases.

L3 ANSWER 3 OF 9 MEDLINE on STN DUPLICATE 2

2005198587. PubMed ID: 15766290. Combined N- and C-terminal truncation of human apolipoprotein A -I yields a folded, functional central domain. Beckstead Jennifer A; Block Brian L; Bielicki John K; Kay Cyril M; Oda Michael N; Ryan Robert O. (Lipid Biology in Health and Disease Research Group, Children's Hospital Oakland Research Institute, 5700 Martin Luther King Jr. Way, Oakland, California 94609, USA. ) Biochemistry, (2005 Mar 22) Vol. 44, No. 11, pp. 4591-9. Journal code: 0370623. ISSN: 0006-2960. Pub. country: United States. Language: English.

AB A combined N- and C-terminal truncation variant of human apolipoprotein A-I (apoA-I) was designed, expressed in Escherichia coli, isolated, and characterized. Hydrodynamic experiments yielded a weight average molecular weight of 34000, indicating apoA-I-(44-186) exists in solution predominantly as a dimer. An axial ratio of 4.2 was calculated for the dimer based on sedimentation velocity experiments. Far-UV circular dichroism spectroscopy of apoA-I-(44-186) in buffer indicated the presence of 65% alpha-helix secondary structure. Guanidine hydrochloride denaturation experiments yielded a transition midpoint of 0.5 M for apoA-I-(44-186). ApoA-I-(44-186) induced solubilization of dimyristoylphosphatidylcholine vesicles at a rate comparable to that of full-length apoA-I, displayed lipoprotein binding ability, and was an acceptor of ABCA1-mediated cholesterol efflux from cultured macrophages. Fluorescence quenching studies with KI indicate that the three Trp residues in apoA-I-(44-186) are shielded from the aqueous environment. Taken together, the data indicate that lipid-free apoA-I-(44-186) adopts a folded conformation in solution that possesses lipid binding capability. The central region of apoA-I appears to adopt a globular amphipathic alpha-helix bundle organization that is stabilized by intramolecular and/or intermolecular helix-helix interactions. Lipid association likely results in a conformational adaptation wherein helix-helix contacts are substituted for helix-lipid interactions.

L3 ANSWER 4 OF 9 MEDLINE on STN DUPLICATE 3

2001116736. PubMed ID: 11123918. Probing the lipid-free structure and stability of apolipoprotein A-I by mutation. Gorshkova I N; Liadaki K; Gursky O; Atkinson D; Zannis V I. (Section of Molecular Genetics at Whitaker Cardiovascular Institute and Department of Biophysics, Boston University School of Medicine, 715 Albany Street, Boston, Massachusetts 02118, USA.. igorshko@bu.edu) . Biochemistry, (2000 Dec 26) Vol. 39, No. 51, pp. 15910-9. Journal code: 0370623. ISSN: 0006-2960. Pub. country: United States. Language: English.

AB To probe the secondary structure of the C-terminus (residues 165-243) of lipid-free human apolipoprotein A-I (apoA-I) and its role in protein stability, recombinant wild-type and seven site-specific mutants have been produced in C127 cells, purified,

and studied by circular dichroism and fluorescence spectroscopy. A double substitution (G185P, G186P) increases the protein stability without altering the secondary structure, suggesting that G185 and G186 are located in a loop/disordered region. A triple substitution (L222K, F225K, F229K) leads to a small increase in the alpha-helical content and stability, indicating that L222, F225, and F229 are not involved in stabilizing hydrophobic core contacts. The C-terminal truncation Delta(209-243) does not change the alpha-helical content but reduces the protein stability. Truncation of a larger segment, Delta(185-243), does not affect the secondary structure or stability. In contrast, an intermediate truncation, Delta(198-243), leads to a significant reduction in the alpha-helical content, stability, and unfolding cooperativity. The internal 11-mer deletion Delta(187-197) has no significant effect on the conformation or stability, whereas another internal 11-mer deletion, Delta(165-175), dramatically disrupts and destabilizes the protein conformation, suggesting that the presence of residues 165-175 is crucial for proper apoA-I folding. Overall, the findings suggest the presence of stable helical structure in the C-terminal region 165-243 of lipid-free apoA-I and the involvement of segment 209-243 in stabilizing interactions in the molecule. The effect of the substitution (G185P, G186P) on the exposure of tryptophans located in the N-terminal half suggests an apoA-I tertiary conformation with the C-terminus located close to the N-terminus.

L3 ANSWER 5 OF 9 MEDLINE on STN DUPLICATE 4
97156790. PubMed ID: 9003180. Truncation of the amino terminus of human apolipoprotein A-I substantially alters only the lipid-free conformation. Rogers D P; Brouillette C G; Engler J A; Tendian S W; Roberts L; Mishra V K; Anantharamaiah G M; Lund-Katz S; Phillips M C; Ray M J. (Biochemistry Department, Southern Research Institute, Birmingham, Alabama 35209, USA. ) Biochemistry, (1997 Jan 14) Vol. 36, No. 2, pp. 288-300. Journal code: 0370623. ISSN: 0006-2960. Pub. country: United States. Language: English.
AB An amino-terminal deletion mutant (residues 1-43) of human apolipoprotein A-I (apo hA-I) has been produced from a bacterial expression system to explore the structural and functional role of these amino acids, encoded by exon 3, in apo hA-I. Lipid binding of apo delta (1-43)A-I and lipid binding of apo hA-I are very similar as assessed by surface activity, lipid association with palmitoyloleoylphosphatidylcholine (POPC) vesicles, and lipid association with plasma lipoproteins. Preliminary kinetic measurements appear to show that the reactivity of lecithin:cholesterol acyltransferase (LCAT) with the mutant is slightly decreased compared to wild-type apo hA-I. Collectively, these results indicate that the N-terminal region is not necessary for lipid binding or activation of LCAT. In contrast, there are significant structural differences between lipid-free apo delta (1-43)A-I and apo hA-I, as judged by denaturant-induced unfolding, binding of the fluorescent probe 1-anilinonaphthalene-8-sulfonate, surface balance measurements, and far- and near-ultraviolet circular dichroic spectroscopy. All spectral and physical measurements indicate apo delta (1-43)A-I has a folded, tertiary structure, although it is significantly less stable than that of apo hA-I. It is concluded that the N-terminal 43 residues are an important structural element of the lipid-free conformational state of apo hA-I, the absence of which induces a fundamentally different fold for the remaining carboxy-terminal residues, compared to those in native apo hA-I.

L3 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
1997:21295 Document No. 126:102076 Efflux of cellular cholesterol and phospholipid to apolipoprotein A-I mutants. Sviridov, Dmitri; Pyle, Louise E.; Fidge, Noel (Baker Medical Research Institute, Prahran, 3181, Australia). Journal of Biological Chemistry, 271(52), 33277-33283 (English) 1996. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.
AB Human plasma apolipoprotein A-I (apoA-I) and recombinant full-length

proapoA-I (apoA-I-(-6-243)) as well as four truncated forms of proapoA-I were used as acceptors to study cholesterol and phospholipid efflux from HepG2 cells. Efflux of both cholesterol and phospholipid to the lipid-free plasma apoA-I was twice that of apoA-I-(6-243). When apoA-I was incorporated into reconstituted high d. lipoprotein, cholesterol afflux increased, and the difference between plasma apoA-I and apoA-I-(6-243) disappeared. Truncation of recombinant ApoA-I to residues 222 (apoA-I-(6-222)) and 210 (apoA-I-(6-210)) resulted in a 70-95% decrease in their ability to promote the efflux of both intracellular and plasma membrane cholesterol. Further truncation to residues 150 (apoA-I-(6-150)) and 135 (apoA-I-(-6-135)) fully restored the ability of apoA-I to promote cholesterol efflux. Phospholipid efflux closely paralleled the efflux of cholesterol. Interaction of 125I-labeled apoA-I with the cells was similar for apoA-I-(-6-243), apoA-I-(-6-222), and apoA-I-(-6-210), but slightly higher for apoA-I-(-6-150) and apoA-I-(-6-135). When complexed with phospholipid, all forms except apoA-I-(-6-210) formed discoidal reconstituted high d. lipoprotein particles. When the same amts. of free or lipid-associated apoA-I were compared, association of apoA-I with phospholipid increased cholesterol efflux and decreased phospholipid efflux, and the difference in the ability of different mutants to promote cholesterol and phospholipid efflux disappeared. We conclude that the capacity of lipid-free apoA-I to promote cholesterol efflux is related to its ability to mobilize cellular phospholipid, which apparently involves a region around residues 222-243. A second lipid-binding region is exposed when the carbonyl-terminal half of apoA-I is absent.

L3 ANSWER 7 OF 9 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
1996:308115 Document No.: PREV199699030471. Truncation of the amino terminus of human apolipoprotein A-I substantially alters only the lipid-free conformation. Rogers, D. [Reprint author]; Ray, M.; Ross, L.; Mishra, V.; Anantharamaiah, G.; Lund-Katz, S.; Phillips, M.; Engler, J.; Brouillette, C.. Univ. Ala. at Birmingham, Birmingham, AL 35294, USA. FASEB Journal, (1996) Vol. 10, No. 6, pp. A1111.
Meeting Info.: Joint Meeting of the American Society for Biochemistry and Molecular Biology, the American Society for Investigative Pathology and the American Association of Immunologists. New Orleans, Louisiana, USA. June 2-6, 1996.
CODEN: FAJOEC. ISSN: 0892-6638. Language: English.

L3 ANSWER 8 OF 9 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
1996:384651 The Genuine Article (R) Number: UK861. Truncation of the amino terminus of human apolipoprotein A -I substantially alters only the lipid-free conformation.. Rogers D (Reprint); Ray M; Ross L; Mishra V; Anantharamaiah G; LundKatz S; Phillips M; Engler J; Brouillette C. UNIV ALABAMA, BIRMINGHAM, AL 35294; MED COLL PENN & HAHNEMANN UNIV, PHILADELPHIA, PA 19129; SO RES INST, BIRMINGHAM, AL 35209. FASEB JOURNAL (30 APR 1996) Vol. 10, No. 6, pp. 651-651. ISSN: 0892-6638. Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998. Language: English.

L3 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
1995:440700 Document No. 122:210470 Carboxyl-terminal domain truncation alters apolipoprotein A-I in vivo catabolism. Schmidt, Hartmut H. J.; Remaley, Alan T.; Stonik, John A.; Roman, Rosemary; Wellmann, Axel; Thomas, Fairwell; Zech, Loren A.; Brewer, H. Bryan, Jr.; Hoeg, Jeffrey W. (Mol. Disease Branch, Natl. Inst. Health, Bethesda, MD, 20892, USA). Journal of Biological Chemistry, 270(10), 5469-75 (English) 1995. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.
AB Apolipoprotein A-I (apoA-I), the major protein of high d. lipoproteins, facilitates reverse, cholesterol transport from peripheral tissue to liver. To determine the structural motifs important for modulating the in vivo

catabolism of human apoA-I (h-apoA-I), the authors generated carboxyl-terminal truncation mutants at residues 201 (apoA-I201), 217 (apoA-I217), and 226 (apoA-I226) by site-directed mutagenesis. ApoA-I was expressed in Escherichia coli as a fusion protein with the maltose binding protein, which was removed by factor Xa cleavage. The in vivo kinetic anal. of the radioiodinated apoA-I in normolipemic rabbits revealed a markedly increased rate of catabolism for the truncated forms of apoA-I. The fractional catabolic rates (FCR) of 9.10/day for apoA-I201, 6.34/day for apoA-I217, and 4.4.2/day for apoA-I226 were much faster than the FCR of recombinant intact apoA-I (r-apoA-I, 0.93/day) and h-apoA-I (0.91/day). All the truncated forms of apoA-I were associated with very high d. lipoproteins, whereas the intact recombinant apoA-I (r-apoA-I) and h-apoA-I associated with HDL2 and HDL3. Gel filtration chromatog. revealed that in contrast to r-apoA-I, the mutant apoA-I201 associated with a phospholipid-rich rabbit apoA-I containing particle. Anal. by agarose gel electrophoresis demonstrated that the same mutant migrated in the pre-β position, but not within the α position as did r-apoA-I. These results indicate that the carboxyl-terminal region (residue 227-243) of apoA-I is critical in modulating the association of apoA-I with lipoproteins and in vivo metabolism of apoA-I.

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=> s l1 and milano
L4          27 L1 AND MILANO

=> s l4 and truncation
L5           0 L4 AND TRUNCATION

=> s l4 and THP-1
L6           4 L4 AND THP-1

=> dup remove l6
PROCESSING COMPLETED FOR L6
L7           1 DUP REMOVE L6 (3 DUPLICATES REMOVED)

=> d l7 cbib abs

L7   ANSWER 1 OF 1     MEDLINE on STN                    DUPLICATE 1
2005251734.    PubMed ID: 15805548.   Cysteine mutants of human
     apolipoprotein A-I: a study of secondary
     structural and functional properties. Zhu Xuewei; Wu Gang; Zeng Wuwei; Xue
     Hong; Chen Baosheng. (Department of Biochemistry and Molecular Biology,
     Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences
     and Peking Union Medical College, Beijing, China 100005. ) Journal of
     lipid research, (2005 Jun) Vol. 46, No. 6, pp. 1303-11.  Electronic
     Publication: 2005-04-01. Journal code: 0376606. ISSN: 0022-2275. Pub.
     country: United States. Language: English.
AB   Apolipoprotein A-I(Milano) (A-I(M)) (R173C), a natural mutant of
     human apolipoprotein A-I (apoA-I),
     and five other cysteine variants of apoA-I at residues 52 (S52C), 74
     (N74C), 107 (K107C), 129 (G129C), and 195 (K195C) were generated.
     Cysteine residues were incorporated in each of the various helices at the
     same helical wheel position as for the substitution in A-I(M).  The
     secondary structural properties of the monomeric mutants, their abilities
     to bind lipid and to promote cholesterol efflux from THP-
     1 macrophages, and the possibility of antiperoxidation were
     investigated.  Results showed that the alpha helical contents of all of
     the cysteine mutants were similar to that of wild-type apoA-I (wtapoA-I).
     The cysteine variant of A-I(M) at residue 173 [A-I(M)(R173C)] exhibited
     weakened structural stability, whereas A-I(G129C) a more stable structure
     than wtapoA-I.  A-I(G129C) and A-I(K195C) exhibited significantly impaired
     capabilities to bind lipid compared with wtapoA-I.  A-I(K107C) possessed a
     higher capacity to promote cholesterol efflux from macrophages than
     wtapoA-I, and A-I(M)(R173C) and A-I(K195C) exhibited an impaired efflux
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capability. Neither A-I(M)(R173C) nor any other cysteine mutant could resist oxidation against lipoxygenase. In summary, in spite of the similar mutant position on the helix, these variants exhibited different structural features or biological activities, suggesting the potential influence of the local environment of mutations on the whole polypeptide chain.

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=> s l4 and HUTs
L8            0 L4 AND HUTS

=> d his

     (FILE 'HOME' ENTERED AT 09:05:30 ON 27 MAR 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 09:05:50 ON
     27 MAR 2007
L1         1678 S HUMAN APOLIPOPROTEIN A-I
L2           25 S L1 AND TRUNCATION
L3            9 DUP REMOVE L2 (16 DUPLICATES REMOVED)
L4           27 S L1 AND MILANO
L5            0 S L4 AND TRUNCATION
L6            4 S L4 AND THP-1
L7            1 DUP REMOVE L6 (3 DUPLICATES REMOVED)
L8            0 S L4 AND HUTS

=> s l1 and T cell activation
L9            2 L1 AND T CELL ACTIVATION

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10           2 DUP REMOVE L9 (0 DUPLICATES REMOVED)

=> d l10 1-2 cbib abs

L10  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2007 ACS on STN
2005:1210854   Document No. 144:21753  Apolipoprotein A-I induces IL-10 and
     PGE2 production in human monocytes and inhibits dendritic cell
     differentiation and maturation.  Kim, Kwang Dong; Lim, Ho Yong; Lee, Hee
     Gu; Yoon, Do-Young; Choe, Yong-Kyung; Choi, Inpyo; Paik, Sang-Gi; Kim,
     Young-Sang; Yang, Young; Lim, Jong-Seok (Department of Biological
     Sciences, Sookmyung Women's University, Seoul, 140-742, S. Korea).
     Biochemical and Biophysical Research Communications, 338(2), 1126-1136
     (English) 2005.  CODEN: BBRCA9.  ISSN: 0006-291X.  Publisher: Elsevier.
AB   Apolipoprotein A-I (apoA-I), the major protein component of serum high-d.
     lipoprotein, exhibits anti-inflammatory activity in atherosclerosis.  In
     this study, the authors demonstrate that apoA-I inhibits DC
     differentiation and maturation.  DC differentiated from monocytes in the
     presence of apoA-the author showed a decreased expression of surface mols.
     such as CD1a, CD80, CD86, and HLA-DR.  In addition, these DC exhibited
     decreased endocytic activity and weakened allogeneic T-
     cell activation.  During DC differentiation in the
     presence of apoA-I, PGE2 and IL-10, which are known to be DC
     differentiation inhibitors and/or modulators of DC function, were produced
     at remarkable rates, whereas IL-12 production in the cells after stimulation
     with CD40 mAb and IFN-γ was significantly decreased in comparison
     with the control DC.  T cells stimulated by apoA-I-pretreated DC produced
     significantly low levels of IFN-γ, and apoA-I inhibited cross-talk
     between DC and NK cells, in terms of IL-12 and IFN-γ production
     Therefore, apoA-I appears to play an important role in modulating both
     innate immune response and inflammatory response.  The novel inhibitory
     function of apoA-I on DC differentiation and function may facilitate the
     development of new therapeutic interventions in inflammatory diseases.

L10  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2007 ACS on STN
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2001:693510 Document No. 135:271905 Apolipoprotein A-I and its fragments regulate T-cell-dependent monocyte activation. Edwards, Carl K., III; Burger, Danielle; Dayer, Jean-Michel; Kohno, Tadahiko (Amgen Inc., USA). PCT Int. Appl. WO 2001068852 A2 20010920, 132 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US7826 20010313. PRIORITY: US 2000-PV189008 20000313.

AB The invention provides apolipoprotein A-I fragment T cell activation inhibitor (AFTI) polypeptides and nucleic acid mols. encoding the same. Apolipoprotein and its fragments are shown to regulate T-cell mediated activation of monocytes via the inhibition of interleukin-1β and tumor necrosis factor-α secretion. A fragment of apo-A-I comprising domains II and III also displays inhibitory activity. The invention also provides vectors, host cells, selective binding agents, and methods for producing AFTI polypeptides. Also provided are methods for the treatment, diagnosis, amelioration, or prevention of diseases with AFTI polypeptides, particularly IL-1 mediated diseases, TNF-α mediated diseases, and diseases involving monocyte activation.

=> s l1 and domain II
L11 1 L1 AND DOMAIN II

=> d l11 cbib abs

L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
2001:693510 Document No. 135:271905 Apolipoprotein A-I and its fragments regulate T-cell-dependent monocyte activation. Edwards, Carl K., III; Burger, Danielle; Dayer, Jean-Michel; Kohno, Tadahiko (Amgen Inc., USA). PCT Int. Appl. WO 2001068852 A2 20010920, 132 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US7826 20010313. PRIORITY: US 2000-PV189008 20000313.

AB The invention provides apolipoprotein A-I fragment T cell activation inhibitor (AFTI) polypeptides and nucleic acid mols. encoding the same. Apolipoprotein and its fragments are shown to regulate T-cell mediated activation of monocytes via the inhibition of interleukin-1β and tumor necrosis factor-α secretion. A fragment of apo-A-I comprising domains II and III also displays inhibitory activity. The invention also provides vectors, host cells, selective binding agents, and methods for producing AFTI polypeptides. Also provided are methods for the treatment, diagnosis, amelioration, or prevention of diseases with AFTI polypeptides, particularly IL-1 mediated diseases, TNF-α mediated diseases, and diseases involving monocyte activation.

=> s l1 and domain III
L12 0 L1 AND DOMAIN III

=> s l1 and receptor binding
L13 13 L1 AND RECEPTOR BINDING

=> dup remove l13
PROCESSING COMPLETED FOR L13
L14 9 DUP REMOVE L13 (4 DUPLICATES REMOVED)

=> d l14 1-9 cbib abs

L14 ANSWER 1 OF 9 MEDLINE on STN DUPLICATE 1
2002702288. PubMed ID: 12462973. The role of structural and functional homology between human apolipoprotein A-I and envelope proteins of human immunodeficiency virus type 1 in CD4 receptor binding. Panin L E; Kostina N E; Lukashev V A. (Institute of Biochemistry, Siberian Division, Russian Academy of Sciences, ul. Akademika Timyakova 2, Novosibirsk, 630117 Russia. ) Doklady. Biochemistry and biophysics, (2002 Jul-Aug) Vol. 385, pp. 209-12. Journal code: 101126895. ISSN: 1607-6729. Pub. country: Russia: Russian Federation. Language: English.

L14 ANSWER 2 OF 9 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
2001:314802 The Genuine Article (R) Number: 419HB. Structural models of human apolipoprotein A-I: a critical analysis and review. Brouillette C G (Reprint); Anantharamaiah G M; Engler J A; Borhani D W. Univ Alabama, Ctr Biophys Sci & Engn, 1918 Univ Blvd, Birmingham, AL 35294 USA (Reprint); Univ Alabama, Ctr Biophys Sci & Engn, Birmingham, AL 35294 USA; Univ Alabama, Atherosclerosis Res Unit, Birmingham, AL 35294 USA; Univ Alabama, Dept Biochem & Mol Genet, Birmingham, AL 35294 USA; BASF Biores Corp, Worcester, MA 01605 USA. BIOCHIMICA ET BIOPHYSICA ACTA-MOLECULAR AND CELL BIOLOGY OF LIPIDS (30 MAR 2001) Vol. 1531, No. 1-2, pp. 4-46. ISSN: 1388-1981. Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. Language: English.
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB Human apolipoprotein (apo) A-I has been the subject of intense investigation because of its well-documented antiatherogenic properties. About 70% of the protein found in high density lipoprotein complexes is apo A-I, a molecule that contains a series of highly homologous amphiphatic alpha -helices. A number of significant experimental observations have allowed increasing sophisticated structural models for both the lipid-bound and the lipid-free forms of the apo A-I molecule to be tested critically. It seems clear, for example, that interactions between amphipathic domains in apo A-I may be crucial to understanding the dynamic nature of the molecule and the pathways by which the lipid-free molecule binds to lipid, both in a discoidal and a spherical particle. The state of the art of these structural studies is discussed and placed in context with current models and concepts of the physiological role of apo A-I and high-density lipoprotein in atherosclerosis and lipid metabolism. (C) 2001 Elsevier Science B.V. All rights reserved.

L14 ANSWER 3 OF 9 MEDLINE on STN DUPLICATE 2
1999320754. PubMed ID: 10392457. Human apolipoprotein E N-terminal domain displacement of apolipophorin III from insect low density lipophorin creates a receptor-competent hybrid lipoprotein. Fisher C A; Kiss R S; Francis G A; Gao P; Ryan R O. (Department of Biochemistry, University of Alberta, Edmonton, Canada. ) Comparative biochemistry and physiology. Part B, Biochemistry & molecular biology, (1999 Apr) Vol. 122, No. 4, pp. 447-51. Journal code: 9516061. ISSN: 1096-4959. Pub. country: ENGLAND: United Kingdom. Language: English.
AB The surface of Manduca sexta low density lipophorin (LDLp) particles was employed as a template to examine the relative lipid binding affinity of the 22 kDa receptor binding domain (residues 1-183) of human apolipoprotein E3 (apo E3). Isolated LDLp was incubated with exogenous apolipoprotein and, following re-isolation by density gradient ultracentrifugation, particle apolipoprotein content was determined. Incubation of recombinant human apo E3(1-183) with LDLp resulted in a saturable displacement of apolipophorin III (apo Lp-III) from the particle surface, creating a hybrid apo E3(1-183)-LDLp. Although subsequent

incubation with excess exogenous apo Lp-III failed to reverse the process, human apolipoprotein A-I (apo A-I)
effectively displaced apo E3(1-183) from the particle surface. We conclude that human apo E N-terminal domain possesses a higher intrinsic lipid binding affinity than apo Lp-III but has a lower affinity than human apo A-I. The apo E3(1-183)-LDLp hybrid was competent to bind to the low density lipoprotein receptor on cultured fibroblasts. The system described is useful for characterizing the relative lipid binding affinities of wild type and mutant exchangeable apolipoproteins and evaluation of their biological properties when associated with the surface of a spherical lipoprotein.

L14 ANSWER 4 OF 9 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

1998:101314 The Genuine Article (R) Number: YU546. Structural analysis of apolipoprotein A-I: Effects of amino- and carboxy-terminal deletions on the lipid-free structure. Rogers D P; Roberts L M; Lebowitz J; Engler J A (Reprint); Brouillette C G. Univ Alabama, Ctr Macromol Crystallog, Birmingham Med Ctr, Dept Biochem & Mol Genet, Birmingham, AL 35294 USA (Reprint); Univ Alabama, Dept Microbiol, Birmingham Med Ctr, Birmingham, AL 35294 USA; Calif State Univ Sacramento, Dept Chem, Sacramento, CA 95819 USA. BIOCHEMISTRY (20 JAN 1998) Vol. 37, No. 3, pp. 945-955. ISSN: 0006-2960. Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA. Language: English.

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB An amino-terminal deletion mutant (residues 1-43) and a carboxy-terminal deletion mutant (residues 187-243) of human apolipoprotein A-I (ape hA-I) have been
produced from a bacterial expression system to explore the importance of the missing residues for the conformation of apo hA-I. Our focus has been to study the lipid-free structure of apo hA-I to understand how discrete domains influence the conformational plasticity of the protein and, by inference, the mechanism of lipid binding. All spectral and physical measurements indicate that both apo Delta(1-43)A-I and apo Delta(187-243)A-I have folded, tertiary structures. These structures differ in the specific arrangement of helical domains based, in part, on their relative thermodynamic stability, near-and far-UV CD, limited proteolysis, and the accessibility of tryptophans to fluorescence quenchers. In addition, all data indicate that the folded domains of apo hA-I and apo Delta(187-243)A-I are very similar. Results from analytical ultracentrifugation suggest that lipid-free apo hA-I and the deletion mutants each exist in a dynamic equilibrium between a loosely folded, helical bundle and an elongated monomeric helical hairpin. The conformational heterogeneity is consistent with significant ANS binding exhibited by all three proteins and could help to explain the facile lipid binding properties of apo hA-I.

L14 ANSWER 5 OF 9 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

93270721 EMBASE Document No.: 1993270721. Regulation of lecithin-cholesterol acyltransferase reaction by acyl acceptors and demonstration of its 'idling' reaction. Czarnecka H.; Yokoyama S.. Lipid/Lipoprotein Research Group, Department of Medicine, University of Alberta,Edmonton, Alta. T6G 2S2, Canada. Journal of Biological Chemistry Vol. 268, No. 26, pp. 19334-19340 1993.
ISSN: 0021-9258. CODEN: JBCHA3
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 931010. Last Updated on STN: 931010

AB The mechanism for regulation of cholesterol esterification by lecithin-cholesterol acyltransferase (LCAT) was studied using the highly isolated enzyme from pig plasma. In the reaction with phosphatidylcholine small unilamellar vesicles, cholesterol, water, diacylglycerol, and lysophosphatidylcholine were all potent acceptors of an acyl group cleaved from the sn-2 position of egg phosphatidylcholine, generating cholesteryl ester, free fatty acid, triglyceride, and phosphatidylcholine,

respectively. All of these reactions required activation by human apolipoprotein A-I, suggesting that this activation leads to the deacylation of phosphatidylcholine. Those acceptors competed against each other in this vesicle reaction system, and cholesterol was the most potent acyl acceptor. Lysophosphatidylcholine that was endogenously generated by deacylation of phosphatidylcholine in the first step of the LCAT reaction was also a good acyl acceptor, showing that the reaction is always partly 'idling'. Bovine serum albumin partially inhibited this idling reaction in a concentration- dependent manner up to 80% at 0.60 mM. The above results were essentially reproducible with high density lipoprotein, except that cholesterol is less potent than lysophosphatidylcholine in accepting the acyl group under the condition used. Unlike the apolipoprotein A-I-activated reaction, cholesterol was esterified only slightly by the LCAT reaction on low density lipoprotein and, consequently, did not compete against lysophosphatidylcholine for generation of phosphatidylcholine. Thus, apoB may activate LCAT in a very different manner from apoA-I. The rate of esterification of lysophosphatidylcholine on low density lipoprotein was one-tenth of that on the vesicles and on high density lipoprotein. Thus, LCAT is active on low density lipoprotein but mostly idling as deacylating and reacylating glycerophospholipids.

L14 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

1993:207951 Document No. 118:207951 Monoclonal antibodies to human apolipoprotein AI: Probing the putative receptor binding domain of apolipoprotein AI. Allan, Charles M.; Fidge, Noel H.; Morrison, John R.; Kanellos, Jerry (Protein Chem. Mol. Biol. Unit., Baker Med. Res. Inst., Prahran, 3181, Australia). Biochemical Journal, 290(2), 449-55 (English) 1993. CODEN: BIJOAK. ISSN: 0306-3275.

AB Four monoclonal antibodies (MAbs) specific for human apolipoprotein (apo) AI, designated AI-1, AI-3, AI-4.1 and AI-4.2, were used to study the interaction between high-d. lipoprotein HDL3 and rat liver plasma membranes. MAbs AI-1 and AI-3 recognize epitopes within residues 28-47 and 140-147, resp., of apoA-I (C. M. Allan, et al, 1991). Two previously unreported MAbs, AI-4.1 and AI-4.2, were raised against purified CNBr fragment 4 (CF4) of apoAI, the C-terminal region. Using ELISA and immunoblotting techniques, it was demonstrated that all four MAbs recognize distinct epitopes within apoAI. Epitope mapping studies using endoproteinase cleavage peptides of CF4 showed that AI-4.1 binds to an epitope within residues 223-233, which is poorly exposed on apoAI mols. associated with lipid. Fab fragments derived from MAb AI-4.2 inhibited the binding of 125I-labeled HDL3 to rat liver plasma membranes, whereas Fab fragments from AI-4.1, AI-3 and AI-1 had little or no effect. In ligand blotting studies with purified CNBr fragments of apoAI and using apoAI-specific antibodies for detection, CF4 showed the highest capacity to recognize two HDL-binding proteins previously identified in rat liver plasma membranes. It was proposed that the specific interaction between HDL and liver plasma membranes is largely mediated through a binding domain in the C-terminus of apoAI, which is consistent with the involvement of specific receptors for the apolipoprotein moiety of HDL.

L14 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

1991:223887 Document No. 114:223887 The amphipathic α-helical repeats of apolipoprotein A-I are responsible for binding of high density lipoproteins to HepG2 cells. Leblond, Lorraine; Marcel, Yves L. (Lab. Lipoprotein Metab., Clin. Res. Inst., Montreal, QC, H2W 1R7, Can.). Journal of Biological Chemistry, 266(10), 6058-67 (English) 1991. CODEN: JBCHA3. ISSN: 0021-9258.

AB Nine monoclonal antibodies (mAbs) against apoA-I reacting with distinct but overlapping epitopes covering more than 90% of the sequence have been used to block the interaction of 125I-labeled high-d. lipoprotein (125I-HDL) with HepG2 cells in order to delineate the cell binding domain of apolipoprotein A-I (apoA-I). While 2 mAbs reacting with epitopes exclusively localized in the N-terminal region (residues 1 to 86) enhanced slightly association of 125I-HDL, all other mAbs, which react with epitopes

localized in the regions of amphipathic α-helical repeats, inhibited that association by 9 to 15%. Although this inhibition is not significant compared to the effect of an irrelevant mAb, combination of these mAbs could significantly inhibit the association of 125I-HDL (32 to 43%) as could polyclonal antibodies (up to 95%). These results are compatible with the concept of HDL binding to these cells via the nonexclusive interaction of each of the amphipathic α-helical repeats of apoA-I. When the same approach was applied to block the association of [3H]cholesteryl ether (CE)-labeled HDL to HepG2 cells, each anti-apoA-I could inhibit by 15 to 25% the cellular association of cholesteryl ether, while mAbs in combination or polyclonal antibodies could inhibit this association up to 45% or 60%, resp. The cholesteryl ether radioactivity that remained associated with the cells (40%) in the presence of polyclonal antibodies could be effectively blocked by addition of an antibody against the receptor-binding domain of apoE (1D7). Therefore, the differential cellular association of cholesteryl ether compared to apolipoprotein can be explained by the presence of apoE secreted by HepG2 and apoE or apoB/E receptors. It is concluded that the optimum uptake of both cholesteryl ether and apoA-I of HDL by cells requires the accessibility of the entire apoA-I and the cooperative binding of the amphipathic α-helical repeats to HepG2 cell membranes. This type of interaction would explain the competitive binding observed for apoA-I, -A-II, and -A-IV by others.

L14 ANSWER 8 OF 9 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

1991:29438 The Genuine Article (R) Number: EQ976. A FRAMESHIFT MUTATION IN THE HUMAN APOLIPOPROTEIN-A-I GENE CAUSES HIGH-DENSITY-LIPOPROTEIN DEFICIENCY, PARTIAL LECITHIN - CHOLESTEROL-ACYLTRANSFERASE DEFICIENCY, AND CORNEAL OPACITIES. FUNKE H (Reprint); VONECKARDSTEIN A; PRITCHARD P H; KARAS M; ALBERS J J; ASSMANN G; RECKWERTH A; WELP S. UNIV MUNSTER, INST KLIN CHEM & LAB MED, ALBERT SCHWEITZER STR 33, W-4400 MUNSTER, GERMANY (Reprint); UNIV BRITISH COLUMBIA, DEPT PATHOL, LIPID RES GRP, VANCOUVER V6T 1W5, BC, CANADA; UNIV MUNSTER, INST MED PHYS, W-4400 MUNSTER, GERMANY; UNIV WASHINGTON, SEATTLE, WA 98105; UNIV MUNSTER, INST ARTERIOSKLEROSEFORSCH, W-4400 MUNSTER, GERMANY. JOURNAL OF CLINICAL INVESTIGATION (JAN 1991) Vol. 87, No. 1, pp. 371-376. ISSN: 0021-9738. Publisher: ROCKEFELLER UNIV PRESS, 222 E 70TH STREET, NEW YORK, NY 10021. Language: English.

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Epidemiologic data of recent years have identified an important role of HDL deficiency in the etiology of atherosclerosis. Biochemical data suggest that some of these deficiencies may be a consequence of defects in the structural genes of HDL apolipoproteins or of plasma enzymes that modify HDL. We analyzed the genetic defect in a 42-yr-old patient suffering from corneal opacities and complete absence of HDL cholesterol but not of coronary artery disease, thus clinically resembling fish eye disease. The observation of an abnormal immunoblot banding pattern of apolipoprotein A-I (apo A-I) and of reduced lecithin: cholesterol acyltransferase (LCAT) activity in plasma led to sequence analysis of the genes for apo A-I and LCAT in this patient and his family. Direct sequencing of polymerase chain reaction amplified DNA segments containing the exons of the candidate genes, resulted in the identification of a frameshift mutation in apo A-I while the LCAT sequence was identical to the wild type, The apo A-I mutation was predictive for an extensive alteration of the COOH-terminal sequence of the encoded protein. Evidence for the release of this mutant protein into the plasma compartment and for the absence of normal apo A-I was derived from ultraviolet laser desorption/ionization mass spectrometry analysis. Our results suggest that a defective apo A-I is the causative defect in this case of HDL deficiency with corneal opacities.

L14 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

1987:30503 Document No. 106:30503 The role of A apolipoproteins in cellular metabolism of high density lipoprotein. Fidge, Noel (Baker Med. Res. Inst., Melbourne, 3181, Australia). International Congress Series,

696(Atherosclerosis 7), 277-80 (English) 1986. CODEN: EXMDA4. ISSN: 0531-5131.

AB The Fab fragments of antibodies to apolipoproteins AI and AII were both capable of suppressing the binding of 125I-labeled human high-d. lipoprotein3, (HDL3) to rat adrenocortical cells, thus suggesting that both AI and AII are the ligands responsible for HDL3 binding. One protein band common to rat adrenocortical, kidney, and liver plasma membranes was identified as the receptor for HDL3 as well as for apolipoproteins AI and AII. This was shown by electrophoresis and subsequent electroblotting followed by incubation with HDL3 or apolipoproteins.

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L16           0 L1 AND "13 KDALTON"

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L19          17 L17 AND 28

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L20            5 DUP REMOVE L19 (12 DUPLICATES REMOVED)

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L20  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2007 ACS on STN
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2005:85120 Document No. 142:275717 A Three-Dimensional Molecular Model of Lipid-Free Apolipoprotein A-I Determined by Cross-Linking/Mass Spectrometry and Sequence Threading. Silva, R. A. Gangani D.; Hilliard, George M.; Fang, Jianwen; Macha, Stephen; Davidson, W. Sean (Department of Pathology and Laboratory Medicine, University of Cincinnati, Cincinnati, OH, 45267, USA). Biochemistry, 44(8), 2759-2769 (English) 2005. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.

AB Apolipoprotein (apo) A-I, a 243-residue, 28.1-kDa protein is a major mediator of the reverse cholesterol transport (RCT) pathway, a process that may reduce the risk of cardiovascular disease in humans. In plasma, a small fraction of lipid-free or lipid-poor apoA-I is likely a key player in the first step of RCT. Therefore, a basic understanding of the structural details of lipid-free apoA-I will be useful for elucidating the mol. details of the pathway. To address this issue, we applied the combined approach of crosslinking chemical and high-resolution mass spectrometry (MS) to obtain distance constraints within the protein structure. The 21 lysine residues within apoA-I were treated with homo bifunctional chemical cross-linkers capable of covalently bridging two lysine residues residing within a defined spacer arm length. After trypsin digestion of the sample, individual peptide masses were identified by MS just after liquid chromatog. separation With respect to the linear amino acid sequence, we identified 5 short-range and 12 long-range cross-links within the monomeric form of lipid-free apoA-I. Using the cross-linker spacer arm length as a constraint for identified Lys pairs, a mol. model was built for the lipid-free apoA-I monomer based on homol. with proteins of similar sequence and known three-dimensional structures. The result is

the first detailed model of lipid-free apoA-I. It depicts a helical bundle structure in which the N- and C-termini are in close proximity. Furthermore, our data suggest that the self-association of lipid-free apoA-I occurs via C- and N-termini of the protein based on the locations of six cross-links that are unique to the cross-linked dimeric form of apoA-I.

L20 ANSWER 2 OF 5 MEDLINE on STN DUPLICATE 1
2004041531. PubMed ID: 14741338. Expression and secretion of human apolipoprotein A-I in the heart. Baroukh Nadine; Lopez Camilo E; Saleh Maria Carla; Recalde Delia; Vergnes Laurent; Ostos Maria A; Fiette Laurence; Fruchart Jean-Charles; Castro Graciela; Zakin Mario M; Ochoa Alberto. (Unite d'Expression des Genes Eucaryotes, Institut Pasteur, Paris, France.. nnbaroukh@lbl.gov) . FEBS letters, (2004 Jan 16) Vol. 557, No. 1-3, pp. 39-44. Journal code: 0155157. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.

AB Various studies have correlated apolipoprotein (apo) A-I, the major component high-density lipoprotein, with protection against development of cardiovascular disease. Although apoA-I expression has been previously detected in the liver and intestine, we have discovered that the human apoA-I gene is also expressed in the heart. Using transgenic (Tg) mice generated with the human apoA-I/C-III/A-IV gene cluster and Tg mice produced with just the 2.2 kb human apoA-I gene, we have detected significant levels of apoA-I expression in the heart. Furthermore, the detection of apoA-I expression in the hearts of human apoA-I Tg mice indicates that the minimal regulatory elements necessary for cardiac expression of the gene are located near its coding sequence. To determine if the apoA-I gene is also expressed in the human heart, similar analyses were performed, where apoA-I expression was found in both adult and fetal hearts. Furthermore in-depth investigation of the various regions of human and Tg mouse hearts revealed that the apoA-I mRNA was present in the ventricles and atria, but not in the aorta. In situ hybridization of Tg mouse hearts revealed that apoA-I expression was restricted to the cardiac myocyte cells. Finally, heart explants and cardiac primary culture experiments with Tg mice showed secretion of particles containing the human apoA-I protein, and metabolic labeling experiments have also detected a 28 kDa human apoA-I protein secreted from the heart. From these novel findings, new insights into the role and function of apoA-I can be extrapolated.

L20 ANSWER 3 OF 5 MEDLINE on STN DUPLICATE 2
91310637. PubMed ID: 1906882. A mutation in the human apolipoprotein A-I gene. Dominant effect on the level and characteristics of plasma high density lipoproteins. Deeb S S; Cheung M C; Peng R L; Wolf A C; Stern R; Albers J J; Knopp R H. (Department of Medicine, University of Washington School of Medicine, Seattle. ) The Journal of biological chemistry, (1991 Jul 25) Vol. 266, No. 21, pp. 13654-60. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Epidemiologic and genetic data suggest an inverse relationship between plasma high density lipoprotein (HDL) cholesterol and the incidence of premature coronary artery disease. Some of the defects leading to low levels of HDL may be a consequence of mutations in the genes coding for HDL apolipoproteins A-I and A-II or for enzymes that modify these particles. A proband with plasma apoA-I and HDL cholesterol that are below 15% of normal levels and with marked bilateral arcus senilis was shown to be heterozygous for a 45-base pair deletion in exon four of the apoA-I gene. This most likely represents a de novo mutation since neither parent carries the mutant allele. The protein product of this allele is predicted to be missing 15 (Glu146-Arg160) of the 22 amino acids comprising the third amphipathic helical domain. The HDL of the proband and his family were studied. Using anti-A-I and anti-A-II immunosorbents we found three populations of HDL particles in the proband. One contained both apoA-I and A-II, Lp(A-I w A-II); one contained apoA-I but no A-II, Lp(A-I w/o A-II); and the third (an unusual one) contained apoA-II but no A-I. Only Lp(A-I w A-II) and (A-I w/o A-II) were present in the plasma of

the proband's parents and brother. Analysis of the HDL particles of the proband by sodium dodecyl sulfate-polyacrylamide gel electrophoresis revealed two protein bands with a molecular mass differing by 6% in the vicinity of 28 kDa whereas the HDL particles of the family members exhibited only a single apoA-I band. The largely dominant effect of this mutant allele (designated apoA-ISeattle) on HDL levels suggests that HDL particles containing any number of mutant apoA-I polypeptides are catabolized rapidly.

L20 ANSWER 4 OF 5 MEDLINE on STN DUPLICATE 3
91099195. PubMed ID: 1702705. The thyroxine-binding site of human apolipoprotein-A-I: location in the N-terminal domain. Benvenga S; Cahnmann H J; Robbins J. (Clinical Endocrinology Branch, National Institute of Diabetes, Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20892. ) Endocrinology, (1991 Jan) Vol. 128, No. 1, pp. 547-52. Journal code: 0375040. ISSN: 0013-7227. Pub. country: United States. Language: English.
AB We tested the ability of nine monoclonal antibodies (MAb) against human apolipoprotein-A-I (apoA-I), the 28.3-kDa major apoprotein of high density lipoproteins (HDL), to inhibit its photoaffinity labeling with [125I]T4. Two forms were evaluated: isolated lipid-free apoA-I (Sigma or Calbiochem) and lipid-complexed apoA-I [HDL2, (density, 1.063-1.125 g/ml) and HDL3 (density, 1.125-1.210 g/ml)]. After labeling with 0.5 nM [125I]T4 in the presence of MAb or normal mouse IgG, the products were analyzed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and subsequent densitometric quantitation of radioactivity associated with the 28 .3-kDa band. Group I MAbs, namely those having epitopes in the N-terminal portion of apoA-I, include MAb 16 (epitopes at residues 1-16), 4 and 14 (residues 1-86), and 18 (residues 98-105); group II includes MAbs 7,10, 15, and 17 (epitopes at residues 87-148); group III includes MAb 9 (residues 149-243). All group I MAbs inhibited [125I]T4 binding to isolated apoA-I with this order of potency: MAb 16 (-50% to -61%) greater than MAb 14 (-37% to -41%) greater than MAb 4 (-27% to -33%) greater than MAb 18 (-19% to -27%). In the case of lipid-associated apoA-I, the pattern of hierarchy was variable, presumably related to the known markedly polydisperse nature of HDL, but a constant feature, in contrast to the case of isolated apoA-I, was that MAb 4 was more potent than MAb 14. Group II MAbs gave less than 3% inhibition in both isolated and lipid-complexed apoA-I. Group III MAb 9 either failed to inhibit or gave 18-27% inhibition (one preparation each of HDL2 and HDL3). We conclude that the T4 site of apoA-I is in the N-terminal domain of apoA-I, closer to the epitope for MAb 16 than to that for MAb 18, and that conformational changes occurring when apoA-I is associated with lipids in the HDL particle alter the spatial relationship between some epitopes and the T4 site. Our definition of the T4 site of apoA-I is consistent with another set of data showing that heparin failed to inhibit [125I]T4 binding to isolated apoA-I. Heparin is known to interact with clusters of basic residues, and these residues are concentrated in the midregion of apoA-I.

L20 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 4
1991:431392 Document No.: PREV199192087557; BA92:87557. TRANSIENT EXPRESSION OF WILD TYPE AND MUTANT HUMAN APOLIPOPROTEIN A -I IN COS CELLS. STOFFEL W [Reprint author]; BINCZEK E. INST BIOCHEMIE, MEDIZINISCHE FAKULTAET, UNIVERSITAET ZU KOELN, JOSEPH-STELZMANN-STR 52, W-5000 KOELN 41, GERMANY. Biological Chemistry Hoppe-Seyler, (1991) Vol. 372, No. 7, pp. 481-488. CODEN: BCHSEI. ISSN: 0177-3593. Language: ENGLISH.
AB A human apolipoprotein AI (apo AI) minigene and two mutants were cloned into the vector pUHD10-1 for expression studies in COS cells under the control of the strong CMV (cytomegalovirus) enhancer and the own apo AI promoter. In the mutated apo AI minigene (mutant M1) the positions of the triplets of Gln-2-Gln-1 at the C-terminus of the prosequence were exchanged against Gln-8-Ala-7, the recognition site of the signal

peptidase of the wild type human apo AI. The prosequence has been deleted in mutant M2 and the presequence linked directly to the N-terminus of the mature apo AI form. We report here on expression studies in COS cells, a cell line, which does not express apo AI. They were transfected by electroporation with pUHD10-1 constructs, which contain (a) the wild type apo AI minigene and (b) the two mutant apo AI minigenes with mutations described above. The following results were obtained: (a) the wild type and mutant apo AI constructs were efficiently transcribed and translated in COS cells, (b) the expression of the wild type preproapo AI minigene in COS cells led to the secretion of proapo AI (29 kDa), that of the mutant (M2) gene, devoid of the prosequence of mature apo AI ( 28.4 kDa), whereas the product of mutant gene M1 (31 kDa) with the recognition site of the signal peptides transposed to the C-terminus of the prosequence remained uncleaved within the COS cells. These in vivo results confirm and extend our previous in vitro expression-translation findings on the processing and secretion using wild type and the same mutations in the preprosequence of human apo AI cDNA constructs. The prosequence of apo AI is neither required for intracellular processing nor secretion. COS cells secreting apolipoprotein AI after transfection offer a system to study the expression and secretion of apolipoproteins and the assembly of lipoprotein particles.

=> s l1 and monocyte
L21 26 L1 AND MONOCYTE

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L22 14 L21 AND CYTOKINE

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PROCESSING COMPLETED FOR L22
L23 6 DUP REMOVE L22 (8 DUPLICATES REMOVED)

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L23 ANSWER 1 OF 6 MEDLINE on STN DUPLICATE 1
2006005054. PubMed ID: 16390275. Elimination of innate immune responses and liver inflammation by PEGylation of adenoviral vectors and methylprednisolone. De Geest Bart; Snoeys Jan; Van Linthout Sophie; Lievens Joke; Collen Desire. (Center for Molecular and Vascular Biology, University of Leuven, 3000 Leuven, Belgium.. bart.degeest@med.kuleuven.de) . Human gene therapy, (2005 Dec) Vol. 16, No. 12, pp. 1439-51. Journal code: 9008950. ISSN: 1043-0342. Pub. country: United States. Language: English.

AB Improvement of the therapeutic index of adenoviral gene transfer requires the development of strategies to abrogate adenoviral capsid-induced inflammation and cytokine production. The effect of monomethoxypolyethylene glycol (MPEG) conjugation to adenoviral vectors and of methylprednisolone (MP) on innate immunity, liver inflammation, and thrombocyte counts was evaluated after transfer of 1011 particles of E1/E3/E4- deleted adenoviral vector expressing human apolipoprotein A-I (apoA-I). Gene transfer with unPEGylated vectors induced peak interleukin-6 (IL-6) plasma levels that were 66-fold above baseline levels in C57BL/6 mice. PEGylation combined with 4 mg of MP 6 hr before and at the time of gene transfer suppressed IL-6 plasma levels to baseline values at all time points. This combination resulted in 24-, 28-, 5.9-, 42-, 26-, and 2.5- fold reduced mRNA expression in the liver of monocyte chemoattractant protein-1, macrophage inflammatory protein-2, interferon-inducible protein-10, macrophage inflammatory protein-1 beta, lipopolysaccharide-induced CXC chemokine, and keratinocyte-derived chemokine, respectively; abrogated neutrophil infiltration in the liver; and reduced alanine aminotransferase levels. PEGylation reduced vector uptake in the spleen and in nonparenchymal liver cells. PEGylation also inhibited the

development of thrombocytopenia. In conclusion, PEGylation of adenoviral vectors combined with MP administration improves the therapeutic index of adenoviral gene transfer.

L23 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
2004:922039 Document No. 142:91932 Apolipoprotein A-I infiltration in rheumatoid arthritis synovial tissue: a control mechanism of cytokine production?. Bresnihan, Barry; Gogarty, Martina; FitzGerald, Oliver; Dayer, Jean-Michel; Burger, Danielle (Department of Rheumatology, St Vincents University Hospital, Dublin, Ire.). Arthritis Research & Therapy, 6(6), R563-R566 (English) 2004. CODEN: ARTRCV. ISSN: 1478-6362. URL: http://arthritis-research.com/content/pdf/ar1443.pdf Publisher: BioMed Central Ltd..
AB The production of tumor necrosis factor α (TNF-α) and interleukin-1β (IL-1β) by monocytes is strongly induced by direct contact with stimulated T lymphocytes, and this mechanism may be critical in the pathogenesis of rheumatoid arthritis (RA). Apolipoprotein A-I (apoA-I) blocks contact-mediated activation of monocytes, causing inhibition of TNF-α and IL-1β production This study examined the hypothesis that apoA-I may have a regulatory role at sites of macrophage activation by T lymphocytes in inflamed RA synovial tissue. Synovial tissue samples were obtained after arthroscopy from patients with early untreated RA or treated RA and from normal subjects. As determined by immunohistochem., apoA-I was consistently present in inflamed synovial tissue that contained infiltrating T cells and macrophages, but it was absent from noninflamed tissue samples obtained from treated patients and from normal subjects. ApoA-I staining was abundant in the perivascular areas and extended in a halo-like pattern to the surrounding cellular infiltrate. C-reactive protein and serum amyloid A were not detected in the same perivascular areas of inflamed tissues. The abundant presence of apoA-I in the perivascular cellular infiltrates of inflamed RA synovial tissue extends the observations in vitro that showed that apoA-I can modify contact-mediated macrophage production of TNF-α and IL-1β. ApoA-I was not present in synovium from patients in apparent remission, suggesting that it has a specific role during phases of disease activity. These findings support the suggestion that the biol. properties of apoA-I, about which knowledge is newly emerging, include anti-inflammatory activities and therefore have important implications for the treatment of chronic inflammatory diseases.

L23 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
2003:777233 Document No. 139:287253 Detection of RNA targets using INVADER oligonucleotide-directed cleavage reactions and construction of modified Thermus polymerase enzymes with thermostable 5'-nuclease activities. Allawi, Hatim; Argue, Brad T.; Bartholomay, Christian Tor; Chehak, Luanne; Curtis, Michelle L.; Eis, Peggy S.; Hall, Jeff G.; Ip, Hon S.; Ji, Lin; Kaiser, Michael; Kwiatkowski, Robert W.; Lukowiak, Andrew A.; Lyamichev, Victor; Lymaicheva, Natalie E.; Ma, Wupo; Neri, Bruce P.; Olson, Sarah M.; Olson-Munoz, Marilyn C.; Schaefer, James J.; Skrzypczynski, Zbigniev; Takova, Tsetska Y.; Thompson, Lisa C.; Vedvik, Kevin L. (USA). U.S. Pat. Appl. Publ. US 2003186238 A1 20031002, 311 pp., Cont.-in-part of U.S. Ser. No. 864,636. (English). CODEN: USXXCO. APPLICATION: US 2002-84839 20020226. PRIORITY: US 1996-756386 19961126; US 1995-381212 19950131; US 1996-599491 19960124; US 1996-682853 19960712; US 1996-759038 19961202; WO 1997-US1072 19970122; US 1997-823516 19970324; US 1999-350309 19990709; US 2000-577304 20000524; US 2001-758282 20010111; US 2001-864636 20010524.
AB The present invention provides novel cleavage agents and polymerases for the cleavage and modification of nucleic acid. The cleavage agents and polymerases find use, for example, for the detection and characterization of nucleic acid sequences and variations in nucleic acid sequences. In some embodiments, the 5'-nuclease activity of a variety of modified Thermus polymerase enzymes is used to cleave a target-dependent cleavage structure, thereby indicating the presence of specific nucleic acid sequences or specific variations thereof. The term "cleavage structure" refers to a structure that is formed by the interaction of at least one

probe oligonucleotide (called the INVADER oligonucleotide) and a target nucleic acid, forming a structure comprising a duplex, the resulting structure being cleavable by a cleavage agent including but not limited to an enzyme. A sample suspected of containing the target sequence is contacted with oligonucleotides capable of forming an invasive cleavage structure in the present of the target sequence and with an agent for detecting the presence of the invasive cleavage structure. ARRESTOR oligonucleotides improve sensitivity of multiple sequential invasive cleavage assays and allow use of higher concns. of primary probe without increasing background signal. The detailed description of the invention includes: (1) detection of specific nucleic acid sequences using 5'-nucleases in an INVADER-directed cleavage assay; (2) signal enhancement by incorporating the products of an invasive cleavage reaction into a subsequent invasive cleavage reaction; (3) effect of ARRESTOR oligonucleotides on signal and background in sequential invasive cleavage reactions; (4) improved enzymes for the use in INVADER oligonucleotide-directed cleavage reactions comprising RNA targets; (5) reaction design for INVADER assay detection of RNA targets; (6) kits for performing the RNA invader assay; and (7) the INVADER assay for direct detection and measurement of specific RNA analytes.

L23 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

2003:435173 Document No. 139:31738 Detection of RNA targets using INVADER oligonucleotide-directed cleavage reactions and construction of modified Thermus polymerase enzymes with thermostable 5'-nuclease activities. Allawi, Hatim; Bartholomay, Christian Tor; Chehak, Luanne; Curtis, Michelle L.; Eis, Peggy S.; Hall, Jeff G.; Ip, Hon S.; Kaiser, Michael; Kwiatkowski, Robert W.; Lukowiak, Andrew A.; Lyamichev, Victor; Ma, Wupo; Olson-Munoz, Marilyn C.; Olson, Sarah M.; Schaefer, James J.; Skrzypczynski, Zbigniew; Takova, Tsetska Y.; Vedvik, Kevin L.; Lyamichev, Natalie; Neri, Burce P. (Third Wave Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 2003104378 A1 20030605, 251 pp., Cont.-in-part of U.S. Ser. No. 758,282. (English). CODEN: USXXCO. APPLICATION: US 2001-864636 20010524. PRIORITY: US 1996-599491 19960124; US 1996-682853 19960712; US 1996-759038 19961202; WO 1997-US1072 19970122; US 1997-823516 19970324; US 1999-350309 19990709; US 2000-381212 20000208; US 2000-577304 20000524; US 2001-758282 20010111.

AB The present invention provides novel cleavage agents and polymerases for the cleavage and modification of nucleic acid. The cleavage agents and polymerases find use, for example, for the detection and characterization of nucleic acid sequences and variations in nucleic acid sequences. In some embodiments, the 5'-nuclease activity of a variety of modified Thermus polymerase enzymes is used to cleave a target-dependent cleavage structure, thereby indicating the presence of specific nucleic acid sequences or specific variations thereof. The term "cleavage structure" refers to a structure that is formed by the interaction of at least one probe oligonucleotide (called the INVADER oligonucleotide) and a target nucleic acid, forming a structure comprising a duplex, the resulting structure being cleavable by a cleavage agent including but not limited to an enzyme. A sample suspected of containing the target sequence is contacted with oligonucleotides capable of forming an invasive cleavage structure in the present of the target sequence and with an agent for detecting the presence of the invasive cleavage structure. ARRESTOR oligonucleotides improve sensitivity of multiple sequential invasive cleavage assays and allow use of higher concns. of primary probe without increasing background signal. The detailed description of the invention includes: (1) detection of specific nucleic acid sequences using 5'-nucleases in an INVADER-directed cleavage assay; (2) signal enhancement by incorporating the products of an invasive cleavage reaction into a subsequent invasive cleavage reaction; (3) effect of ARRESTOR oligonucleotides on signal and background in sequential invasive cleavage reactions; (4) improved enzymes for the use in INVADER oligonucleotide-directed cleavage reactions comprising RNA targets; (5) reaction design for INVADER assay detection of RNA targets; (6) kits for performing the RNA invader assay; and (7) the INVADER assay for direct detection and measurement of specific RNA

analytes.

L23 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
2001:868661 Document No. 136:49292 Detection of RNA targets using INVADER oligonucleotide-directed cleavage reactions and construction of modified Thermus polymerase enzymes with thermostable 5'-nuclease activities. Allawi, Hatim; Bartholomay, Christian Tor; Chehak, Luanne; Curtis, Michelle L.; Eis, Peggy S.; Hall, Jeff G.; Ip, Hon S.; Kaiser, Michael; Kwiatkowski, Robert W., Jr.; Lukowiak, Andrew A.; Lyamichev, Victor; Ma, Wupo; Olson-Munoz, Marilyn C.; Olson, Sarah M.; Schaefer, James J.; Skrzypczynski, Zbigniew; Takova, Tsetska Y.; Vedvik, Kevin L.; Lyamichev, Natalie E.; Neri, Bruce P. (Third Wave Technologies, Inc., USA). PCT Int. Appl. WO 2001090337 A2 20011129, 1266 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US17086 20010524. PRIORITY: US 2000-577304 20000524; US 2001-758282 20010111; US 2001-864426 20010524; US 2001-864636 20010524.

AB The present invention provides novel cleavage agents and polymerases for the cleavage and modification of nucleic acid. The cleavage agents and polymerases find use, for example, for the detection and characterization of nucleic acid sequences and variations in nucleic acid sequences. In some embodiments, the 5'-nuclease activity of a variety of modified Thermus polymerase enzymes is used to cleave a target-dependent cleavage structure, thereby indicating the presence of specific nucleic acid sequences or specific variations thereof. The term "cleavage structure" refers to a structure that is formed by the interaction of at least one probe oligonucleotide (called the INVADER oligonucleotide) and a target nucleic acid, forming a structure comprising a duplex, the resulting structure being cleavable by a cleavage agent including but not limited to an enzyme. A sample suspected of containing the target sequence is contacted with oligonucleotides capable of forming an invasive cleavage structure in the present of the target sequence and with an agent for detecting the presence of the invasive cleavage structure. ARRESTOR oligonucleotides improve sensitivity of multiple sequential invasive cleavage assays and allow use of higher concns. of primary probe without increasing background signal. The detailed description of the invention includes: (1) detection of specific nucleic acid sequences using 5'-nucleases in an INVADER-directed cleavage assay; (2) signal enhancement by incorporating the products of an invasive cleavage reaction into a subsequent invasive cleavage reaction; (3) effect of ARRESTOR oligonucleotides on signal and background in sequential invasive cleavage reactions; (4) improved enzymes for the use in INVADER oligonucleotide-directed cleavage reactions comprising RNA targets; (5) reaction design for INVADER assay detection of RNA targets; (6) kits for performing the RNA invader assay; and (7) the INVADER assay for direct detection and measurement of specific RNA analytes.

L23 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 2
94041636. PubMed ID: 8225591. Prevention of endotoxin-induced monokine release by human low- and high-density lipoproteins and by apolipoprotein A-I. Flegel W A; Baumstark M W; Weinstock C; Berg A; Northoff H. (Abteilung fur Transfusionsmedizin, Universitat Ulm, Germany. ) Infection and immunity, (1993 Dec) Vol. 61, No. 12, pp. 5140-6. Journal code: 0246127. ISSN: 0019-9567. Pub. country: United States. Language: English.

AB Interaction of endotoxin (lipopolysaccharide [LPS]) with human lipoproteins is known to prevent the LPS-induced activation of human monocytes and release of cytokines (monokines). LPS was exposed to lipoprotein classes separated by ultracentrifugation and to apolipoprotein A-I. Then monocytes were added, and the LPS

activation of monocytes was determined by measuring the induced monokines. Failure of LPS to induce monokine release was called LPS inactivation caused by lipoproteins or apolipoproteins. The LPS inactivation is shown to be a function of low-density lipoproteins. High-density lipoproteins inactivate LPS to a much lesser extent. The very-low-density lipoproteins cannot inactivate LPS. Lipid components seemed not absolutely required for LPS inactivation, because purified human apolipoprotein A-I without its physiological lipid complement also inhibits LPS-induced monokine release.

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L24 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
2001:693510 Document No. 135:271905 Apolipoprotein A-I and its fragments regulate T-cell-dependent monocyte activation. Edwards, Carl K., III; Burger, Danielle; Dayer, Jean-Michel; Kohno, Tadahiko (Amgen Inc., USA). PCT Int. Appl. WO 2001068852 A2 20010920, 132 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US7826 20010313. PRIORITY: US 2000-PV189008 20000313.
AB The invention provides apolipoprotein A-I fragment T cell activation inhibitor (AFTI) polypeptides and nucleic acid mols. encoding the same. Apolipoprotein and its fragments are shown to regulate T-cell mediated activation of monocytes via the inhibition of interleukin-1β and tumor necrosis factor-α secretion. A fragment of apo-A-I comprising domains II and III also displays inhibitory activity. The invention also provides vectors, host cells, selective binding agents, and methods for producing AFTI polypeptides. Also provided are methods for the treatment, diagnosis, amelioration, or prevention of diseases with AFTI polypeptides, particularly IL-1 mediated diseases, TNF-α mediated diseases, and diseases involving monocyte activation.

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